

# Journal of Neurotrauma

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## **A systematic review of clinical outcome trajectories from 3 to 12 months following mild or moderate traumatic brain injury.**

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**Abstract:** Our objective was to determine the extent to which clinical outcomes at 3 months predict the 6-to-12-month trajectory in people presenting with mild or moderate traumatic brain injury (TBI). We conducted a systematic review following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and searched MEDLINE, EMBASE, EBSCO, the Web of Science Citation Index from 2005 until May 2025. All observational or interventional study designs which reported clinical outcomes in patients at 3 months, and at a later timepoint, following mild or moderate traumatic brain injury were eligible for inclusion. Two authors independently selected and extracted data. Risk of bias was assessed using the Downs and Black Checklist.

Thirty studies (29 observational, 1 interventional) involving 7993 patients (7781 with mild TBI) met the inclusion criteria. Study quality was variable and heterogeneity in study inclusion criteria and outcome reporting precluded meta-analyses and identification of patient and injury predictors of post 3-month outcome trajectory. Vulnerable populations - including older adults, those with pre-existing cognitive impairment, psychiatric illness or intoxication – were frequently excluded. Analysis of the four most commonly reported outcome measures (RPQ, GOSE, SF-36 and QOLIBRI) – revealed symptom and functional improvement over time, particularly from hospital discharge to 3 months post injury. However substantial problems persist thereafter with 21% to 65% of patients continuing to experience symptoms or impairment depending on cohort and outcome measure. The small number of patients with moderate TBI precluded comparison of outcomes to patients with mild TBI. To improve clinical care, research and patient experience future targeted studies should identify factors determining the post TBI outcome trajectory.

#### Review registration

**PROSPERO REGISTRATION** Carl Marincowitz, Fiona Lecky, Abdullah Pandor, Ruth Wong, Lindsay Wilson. A systematic review of functional outcomes 12 months after mild or moderate traumatic brain injury. PROSPERO 2024 Available from <https://www.crd.york.ac.uk/PROSPERO/view/CRD42021264931>

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**Background**

Traumatic brain injury (TBI) is an alteration of brain function or other evidence of brain pathology due to an external force. It is a major global cause of disability and mortality with over 50 million new cases annually.<sup>1</sup> Existing research and clinical guidelines in acute care heavily focus on the initial clinical identification and treatment of life-threatening injuries in patients with severe TBI.<sup>2</sup> However, over 95% of patients present with an initial Glasgow Coma Scale (GCS) greater than 8 and are conventionally defined as having mild (GCS 13-15) or moderate TBI (GCS 9-12).<sup>2-4</sup> Only around 1% of patients with mild TBI have life threatening injuries and most patients are discharged directly from the Emergency Department without further follow-up or treatment.<sup>5</sup> However, there is growing evidence that many patients with mild TBI may have significant ongoing functional impairment and disability within the first year of injury.<sup>5</sup> Furthermore, healthcare services may not currently adequately address problems that persist after mild and moderate injuries.

Limited evidence exists on how outcomes evolve in the first year following injury and how early outcomes (at 3 months) predict longer-term outcomes. Two previous reviews only included three and five studies respectively, that assessed functional and other outcomes at 3-months following mild TBI.<sup>6,7</sup> The 2014 review by Carroll et al<sup>6</sup> focussing mainly on cognitive function post mild TBI found early post discharge cognitive deficits on a variety of instruments. However, there was conflicting evidence of persistence beyond 3 months post injury. The 2022 review of mild TBI in older adults (> 60 years) by Hulme et al<sup>7</sup> suggested that at least one third had not fully recovered functional outcomes at 6 months post injury. Outcomes for people who have sustained moderate TBI are not well represented in research as their outcomes are often assessed in combination with people who have sustained severe TBI for the prediction of outcomes at single time points.<sup>8</sup> In order to understand gaps in service provision for people who have sustained mild and moderate TBI better understanding of the post acute evolution of clinical outcomes is required. In addition, there is increasing awareness that outcomes beyond the first 3-6 months after TBI are important.

Our systematic review therefore aimed to:

- 1) Describe clinical outcomes following mild and moderate TBI at 3 months post-injury.
- 2) Assess the relationship between clinical outcomes at 3-months and outcomes at 6-12 months post injury.

**Methods**

A systematic review was undertaken in accordance with the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42021264931).<sup>9,10</sup>

*Eligibility criteria*

All observational or interventional study designs focusing on TBI were eligible for inclusion. The study population of interest consisted of people presenting to the Emergency Department or similar acute hospital setting with an initial GCS of 9-15, aged 16 or over who sustained head injury with associated signs/symptoms of TBI (defined as injury to the brain or alteration of brain function due to an external force). Although there are a wide number of scales that have been developed to assess disability, impairment and function as well as quality of life measures following TBI, the following commonly used and validated measures were included: Glasgow Outcome Scale (GOS) and

extended Glasgow Outcome Scale (GOSE); Rivermead Post-concussion Symptoms Questionnaire (RPQ), Short Form 36 Health Survey (SF-36) and Short Form 12 Health Survey (SF-12), EuroQol- 5 Dimension (EQ-5D) and the Quality of Life after Brain Injury (QOLIBRI) questionnaire. These include the major “outcome” Common Data Elements recommended by the International Traumatic Brain Injury Research Initiative supported by the European Community (EC) and US National Institutes of Health (NIH).<sup>11</sup> Whilst most of the aforementioned assess quality of life and ability to function the RPQ was devised to gauge the severity of post concussion symptoms. The range of symptoms assessed in the RPQ encompasses physical (e.g. headache, fatigue) emotional (e.g. feeling irritable or depressed) and cognitive (e.g. difficulty concentrating, forgetfulness) domains of post TBI lived experience. The patient is asked to rate the degree to which each of the 16 symptoms are more of a problem compared with before the injury, using values from 0 to 4 (0=no symptom 1= no worse than before injury, 2/3/4= new or worse mild/moderate/severe post injury symptom). Symptom scores of 1 are not included in the total score. The RPQ total score ranges from 0-64. All outcomes had to be assessed at 3 months and later time points at or within 12 months of injury -to evaluate how impairment persisted and developed. We excluded case-reports, narrative reviews, editorials and opinions, non-human/ biological studies, abstracts or conference presentations with insufficient detail for data extraction and studies not reporting outcomes of interest. Non-English language studies were also excluded.

#### *Data sources and searches*

To reflect the implementation of international TBI guidelines (such as the first NICE head injury guideline),<sup>2,12</sup> - which since 2005 have led to more liberal CT imaging and to recommendations for treatment pathways for patients with mild TBI -we included publications from 1<sup>st</sup> January 2005 to May 2025. We searched the following electronic databases ~~from 1<sup>st</sup> January 2005 to May 2025~~: MEDLINE (Ovid), EMBASE (Ovid), Cumulative Index to Nursing and Allied Health Literature (EBSCO) and Web of Science Core Collection Social Sciences Citation Index (Clarivate Analytics). Searches were supplemented by hand-searching the reference lists of all relevant studies including existing systematic reviews assessing outcomes following TBI,<sup>5,13-16</sup> forward citation searching of relevant articles, and undertaking targeted searches of the World Wide Web using the Google search engine. Further details on the search strategy can be found in Supplementary Material 1.

All identified citations from the electronic searches and other resources were imported into and managed using the EndNote bibliographic software (version 21; Clarivate Analytics, Philadelphia, PA, USA).

#### *Study selection*

Three reviewers (CM, TS, and MT) independently completed title and abstract screening. Full reports of studies potentially meeting the inclusion criteria were retrieved and examined independently by four reviewers (CM, FL, TS and MT). Retrieved full reports that did not meet the inclusion criteria were excluded with documented reasons. Any disagreements were resolved through discussion or arbitration by a topic expert (FL) and included by consensus.

#### *Data extraction and quality assessment*

For eligible studies, data relating to study design (e.g. study details, sample size, population characteristics, presence of injuries on CT imaging, follow-up), methodological quality and outcomes (e.g. functional outcome measures, predictive factors assessed and association with outcomes) were

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extracted by one reviewer (CM) into a standardised data extraction form and independently checked for accuracy by a second reviewer (TS or MT). Any discrepancies were resolved through discussion, or if this was unsuccessful, wider group opinion was sought (FL).

The methodological quality of each included study was assessed using the Downs and Black checklist<sup>17</sup> for randomised and non-randomised studies. The checklist consists of 27 items across five domains: study quality, external validity, study bias, confounding and selection bias and power of the study. Twenty-six items were either answered yes (assigned a score of 1) or no/unable to determine (assigned a score of 0), and one item was scored yes (2), partially (1), or no (0), resulting in a maximum of 28. Methodological quality was classified as “excellent” if studies had a score of 26 or higher, “good” if scores ranged between 20 and 25, “fair” if they ranged between 15 and 19, and “poor” if the score was 14 or lower.<sup>17</sup>

*Data synthesis and analysis*

Due to significant levels of heterogeneity between studies (study design, participants, inclusion criteria, outcome measurements) and variable reporting of items, a meta-analysis was not considered feasible. As a result, a pre-specified narrative synthesis approach was undertaken, with data being summarised in tables with accompanying narrative summaries that included a description of study characteristic, the included variables, and effect estimates, where applicable.<sup>10</sup>

*Patient and Public Involvement and Engagement (PPIE)*

Our authorship includes a scientific commentator and -TBI Researcher - with lived experience as a TBI Survivor (JP) - who critically reviewed the manuscript drafts and approved the final version for submission.

*Ethics statement*

The published PROSPERO protocol for secondary analysis of anonymized data from eligible published studies<sup>10</sup> does not require separate ethical review. All included studies had appropriate ethical review.

**Results**

*Study flow*

Fig 1 summarises the process of identifying and selecting relevant literature. A total of 1,561 unique records underwent title and abstract screening and the full texts of 94 articles was further assessed. Of these, 30 studies met the review eligibility criteria.<sup>18-47</sup> The majority of the articles were excluded primarily for not having useable or relevant outcome data or an inappropriate study population. A full list of excluded studies with reasons for exclusion is provided in Supplementary Material 2.

### Study and patient characteristics

Study characteristics are summarized in Supplementary Material 3. The 30 included studies comprised 29 longitudinal cohort studies and one pilot randomised controlled trial<sup>18-47</sup>. Three papers reported separate RPQ outcomes from the same cohort study<sup>23,24,39</sup> and were appraised independently; therefore, the 30 papers describe 28 separate cohorts. Nine studies were conducted in Europe (including the UK), 13 in the USA, three studies (5 publications) in Australia or New Zealand, one study in Indonesia, one study in Tunisia and one study in Taiwan. Six studies were conducted on patients enrolled in the National Institute of Health (NIH) funded Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) programme, however these studies differed, with albeit sometimes overlapping, patient cohorts and/or reported different outcomes so were assessed separately.<sup>27-30,38,40</sup> The included studies encompassed 7,993 unique patients of whom 179 (2.2%) patients had moderate TBI (presenting GCS 9-12), 33 patients had either mild (presenting GCS 13-15) or moderate TBI<sup>35</sup> (0.4%) and 7,781 patients had mild TBI (mTBI). All studies solely included patients who had presented to the hospital emergency department of -or- were transferred into - a specialist neuroscience or high-level/high-level trauma centre within 48 hours of injury, and were invited for post discharge follow up. The mild TBI cohort studies exhibited considerable heterogeneity in- inclusion criteria as regards to age at presentation, duration of any loss of consciousness and post traumatic amnesia. Exclusion criteria were even more heterogenous as regards- to the presence of intoxication at presentation, any past history of -substance addiction, neurodegenerative or psychiatric conditions, previous TBI, having indications for CT brain scan, CT findings, -and- the ability to speak the local language, consent to and engage with follow up (Supplementary material 4).

### Quality assessment

A detailed assessment of the quality of the each included studies can be found in Supplementary Material 3 Table S4 4. In general, 20 studies<sup>19-27,31-36,39,43-46</sup> were rated as poor quality and ten studies<sup>18,28-30,37,38,40-42,47</sup> as fair using the Downs and Black checklist.<sup>17</sup> Table 1 presents the overall score for each study. Studies tended to score poorly on measures demonstrating internal and external cohort representativeness, sufficient power to detect meaningful differences and adjustment for confounders in analyses of outcome.

### Effect on outcomes

Table 2 presents the twelve outcomes meeting the inclusion criteria that were reported across the included studies. The Rivermead Post Concussion Symptoms Questionnaire and Glasgow Outcome Scale (GOS) or extended version (GOSE) were the most frequently reported outcome measures, and these two outcomes alongside the Short Form-36 Health Survey and Quality of Life after Brain Injury outcome measures were reported in three or more studies constituting both clinical evaluation and patient reported outcomes. Heterogeneity of study design and limited reporting of study information prevented meta-analysis.

### Rivermead Post concussion Symptoms Questionnaire (RPQ)

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Fifteen studies reported the RPQ as an outcome and the findings are summarised in Table 3. Table 3 demonstrates that the studies identified usually reported mean or median RPQ scores sometimes with standard deviations (SD) or interquartile ranges (IQR). In addition, the questionnaire results are also reported as percentages of the study cohort with any, >1, or >2 new symptoms (scores of 2 or more), or the mean/median number of symptoms (scores of 2 or more) being experienced. The two largest studies Kraus et al (N=2005) and Machamer et al (N=1563) reported mean RPQs of 7.3 and 14.2 at 3 months, and 3.6 and 12.9 at 6 months respectively. The inclusion criteria in the study by Kraus et al was limited to patients aged 16-64 and with symptoms indicating presence of mTBI, whilst Machamer et al included all patients aged over 17, and all patients who underwent CT head imaging.<sup>40</sup> The higher RPQ scores – indicating a higher symptom burden - reported by Machamer et al may reflect these differences. One study solely assessed 13 emotional or cognitive RPQ symptom elements<sup>19</sup>.

Table 3 illustrates considerable variation in RPQ outcomes with the highest mean RPQ score at 3-months (30.7) reported in Roy<sup>44</sup> et al for a subgroup (n=49) of mild TBI patients who met criteria for CT head imaging and who had depressive symptoms. The reported RPQ increased at 6-months (32.3) in these patients and is 10 fold greater than the mean 6 month RPQ score in Kraus et al.<sup>26</sup> Whereas the majority of included studies (12 of 15) reported 6 month outcomes the minority reported 12 months outcomes (7 of 15) with 3 fold variation in the mean RPQ score<sup>25,27</sup> (5.1 to 15.9) . One smaller study reported a 24 month mean RPQ of 10.9<sup>20</sup> . The prevalence of new symptoms at 3 months ranged from were 22% > 3 new symptoms<sup>21</sup> to 73% with > 1 new symptom<sup>32</sup>.

Across studies the largest reductions in symptom burden were reported between discharge/early outcomes and 3-months. Small reductions and even increases were reported in RPQ scores between 3-months, 6-months and 1-year<sup>32,41</sup>. This indicated that patients with post-concussion symptoms at 3-months were likely to continue to be symptomatic at later time points ranging from 21-52% prevalence in those followed up<sup>21-23</sup>.

Glasgow Outcome Scale Extended/Glasgow Outcome Scale (GOSE/GOS)

Fourteen studies reported the GOSE or GOS as an outcome and the findings are summarised in Table 4. The two largest studies were Nelson et al (N=1154) and Voormolen et al (N=1104). In a cohort of mTBI patients who met criteria for CT head imaging, Nelson et al reported that 64% of patients had a GOSE<8 at 3 months, 60% at 6 months and 53% at one year. Voormolen et al reported that in a cohort of mTBI patients who underwent CT imaging in those with no intracranial injuries 23% had a GOSE<7 at 3-months 16% had GOSE<7 at 6-months compared to 41% GOSE<7 at 3-months and 35% GOSE<7 at 6-months in those with injuries identified on imaging.

The lowest mean score at 3 months (GOS= 3 equivalent to GOSE 3-4) was reported by Al Fauzi et al in 32 patients with moderate TBI recruited in Tunisia, which increased to 3.5 at 6 months. A mean GOSE of 8 at 3 months was reported for a sub-population of mTBI patients identified as having a good recovery trajectory in Chiang et al which contrasted to a mean GOSE of 7 at 3-months in patients who had initial functional impairment. All studies identified that a proportion of patients had some functional impairment at 6 or 12 months as indicated by a GOSE<8.

Short Form-36 Health Survey (SF-36)

Five studies reported outcomes for the SF-36 (Table 5). Four studies reported outcomes for the physical and mental component summaries (PCS, MCS), and one study reported outcomes for the vitality section. The largest study, Voormolen et al (N=1104), found mTBI patients with injuries identified on CT imaging to have lower mean physical and mental component summary scores at 3 and 6 months post injury than patients without injuries identified on CT.

#### Quality of after Life Brain Injury Scale (QOLIBRI)

Three studies reported outcomes for the QOLIBRI (Table 6). Chiang et al presented mean scores on the 1-5 scale across the 6 domains whilst the other two studies converted these scores to a 1-100 scale. Chiang et al identified two different recovery pathways in a cohort of 100 patients. Patients with impaired quality of life at three months continued to with impairment at 6 months, however by 12 months the difference in symptom burden between the two groups had resolved.

#### Other outcomes

Eight other outcomes were reported in either one or two of the included studies (Table 2). Of these only the Check list of Post concussion syndromes (N=100), EuroQol 5 Dimension 5 Level Survey (N=182), Acute Concussion Evaluation Score (N=260) and Fatigue Severity Scale (N=159) were reported for 100 or more patients.

#### Predictive factors

Fourteen studies identified factors which may be associated with clinical outcomes at 3 months and later time points (Table 7).<sup>22-25,27,29,33-35,37,38,43,45,46</sup> By stratifying patients by CT findings, two of the larger studies Voormolen et al (N=1104) and McMahon et al (n=348) found that patients with injuries identified on CT imaging had statistically significantly worse clinical outcomes and a higher symptom burden at 3 months compared to patients without injuries identified on imaging. However, the differences in reported outcomes between those with injuries and without injuries identified on CT imaging narrowed and even resolved for some outcomes measures at later time points. Five studies reported multivariable models.<sup>24,25,27,34,38</sup> Psychiatric history/symptoms were identified as independently associated with 3-month and longer-term outcomes in three of these studies. Other factors identified in single studies as independently associated with outcomes – particularly GOSE – included: initial injury severity (reflected by GCS or CT findings), ethnicity, years in education, duration of post traumatic amnesia, history of previous migraines, female sex and social deprivation. Three studies stratified outcome analysis by age.<sup>33,35,45</sup> These suggest that although older adults may not have greater impaired function or high symptom burden than younger adults, the nature of their symptoms and impairment differed.

#### Trajectory of outcomes over time

Across studies reporting the RPQ, GOSE, SF-36 and QOLIBRI the majority showed evidence of improvement over time: RPQ 15/15 studies, GOSE 12/14 studies, SF-36 5/5 and QOLIBRI 3/3 studies. Two studies recorded worsening RPQ symptom burden, one study worsening of the SF36 PCS and one worsening of GOSE over time in 13-23% of patients.<sup>22,32,41,47</sup> The largest reported improvements occurred between early assessments (whilst in hospital or at discharge) and

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outcomes measured at 3-months. Across all four outcome measures significant persistent symptom burden, impairment of function, or of quality of life was reported at 6 and 12 months. Notably, between 20 and 50% of patients were reported to have post-concussion symptoms at 6 and 12 months.<sup>23-25,31,39</sup> Over half of patients were reported to have GOSE less than 8 and around 1/3 less than 7 at these time points.<sup>30,31,37</sup> Voormolen et al found that over 20% of patients had impairment that affected daily quality of life as measured by SF-36 and QOLIBRI at 6 months. No single study conducted a multivariable analysis predicting outcome -trajectory beyond 3 months (Table 7). Two of the -smaller studies (< 200 patients) conducted multilevel multivariable models with time of follow up as predictor<sup>22,46</sup> identifying demographics -(age, gender) -and -social determinants of health (employment and insurance status/ area deprivation) as significant. Three larger studies modelled change over time and characterised trajectories by age<sup>31</sup> (not predictive), -CT findings<sup>37</sup> -(not predictive) and extent of depressive symptoms<sup>44</sup> (predictive of poorer PCS recovery) -in univariable analyses.

## Discussion

### *Summary*

We conducted a systematic review characterising the trajectory of clinical outcome following mild and moderate TBI. Whereas previous reviews have estimated prevalence of symptom burden at single timepoints identifying factors associated with increased impairment or characterised the early trajectory of recovery (within 3-months of injury)<sup>5,14-16</sup> we included a specific focus on the change in outcome between 3 months and later time points. Across four commonly reported outcome measures (RPQ, GOSE, SF-36 and QOLIBRI) we have found that disease burden reduced over time, particularly from discharge to 3 months post injury. However, a significant proportion of patients (between 22% and 70% depending on cohort and outcome measure) had 'symptoms or impairment at 3 months with little resolution (21 to 65% with symptoms or impairment) and worsening for some at 6 and 12 months follow up.

### *Strengths and limitations*

Our systematic review reports a search strategy encompassing four electronic databases and we found 30 studies with 28 separate cohorts that met the inclusion criteria. Our review includes all relevant AMSTAR systematic review checklist quality domains apart from a formal assessment of risk of publication bias (item 10), of included studies.<sup>48</sup> However, the nature of our research question (assessing prevalence of symptom burden trajectory) and non-interventional nature of the majority of the studies included makes our review less susceptible to publication bias.

Our review is limited by the nature of the studies identified which met the inclusion criteria. Outcomes for only 179 patients solely with moderate TBI could be identified across the included studies compared to 7,781 patients with mTBI, which prevents any meaningful comparison of the trajectory of recovery between these two groups. Differences in outcome measures used in different studies and how the same outcome was reported prevented meta-analysis and affected the accuracy with which recovery trajectories could be described. The majority (20/30) included studies were found to have poor quality using our quality assessment tool, which again weakens the strength of conclusions which can be drawn from our narrative synthesis – most studies did not report a sampling strategy or screening log, limiting assessment of internal validity versus eligible individuals with moderate or mTBI presenting to the Emergency Department. One study suggested about 8% whilst a second in older adults suggested 72% of those approached with mTBI consented to enrollment in the ED – both studies did not report the characteristics of those not enrolled.<sup>21</sup> The supplementary data extraction table 3 reflects follow up rates at 3 months as a proportion of those initially consenting, and 6 and/or 12 month follow up rates as a proportion of the 3-month cohort. For both rates are generally high (generally over 50%, with many at or close to 100%) however some studies only included patients with at least one or complete follow up across time points<sup>20,37,38</sup>. Furthermore many studies excluded vulnerable populations who frequently present with TBI; such as those with; pre-existing dementia,<sup>14,18,19,22,35,41-3,45,47</sup> older adults,<sup>18,19,22,23,26</sup> people with previous psychiatric illness,<sup>20,34,42,46,47</sup> intoxicated at the time of injury and/or history of substance abuse<sup>22-24,34,39,42,43,47</sup> or patients with injuries on CT brain scan.<sup>19,22-24,27,39,41,43</sup> These exclusions limit the external validity of findings; many studies attempted to compensate for this by enrolling people with extracranial injuries or uninjured - as "control" cohorts<sup>19,20,22,24,26,30,39,40,42,45</sup> - nevertheless the heterogeneity of study inclusion criteria within the definitions of mild and moderate TBI is notable.

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Consistent well-matched controls allow more reliable attribution of PCS symptoms (such as headache) to TBI versus other conditions that occur in the non TBI population (such as a viral infection or mental health problems). However, identifying controls is difficult if not impossible for vulnerable TBI populations such as those with pre-injury dementia or intoxication who sustain TBI though ground level falls. Given the significant disease burden<sup>1</sup> prognostic studies including these vulnerable populations – even without controls - are still of value.

A further limitation concerns the reporting of outcomes. Whilst dichotomising an ordinal scale like the GOSE can facilitate outcome analysis (table 4) -it can also lead to a significant loss of information as GOSE of 7 ("good recovery" with minor persisting problems) represents a vastly different clinical reality than a GOSE of 5 or 6 (moderate disability). By grouping these patients, the true spectrum of disability is obscured. This common practice of binary reporting prevents a nuanced understanding of functional recovery trajectories which should be addressed in future research.<sup>1</sup>

Although 12 outcome measures were assessed across included studies, only 4 outcomes were assessed in over 1000 patients (RPQ, GOSE, SF-36 and QOLIBRI). Therefore, our description of recovery trajectory is characterised best by these outcome measures. An aim of our study was to assess how outcomes at 3 months impacted on later outcomes and identify factors which affected this trajectory. Although some studies identified risk factors for outcomes measured at single time points, no study identified factors which affected trajectory in multi-variable models. However, Voormolen<sup>37</sup> et al stratified recovery trajectory by presence of injuries identified on CT imaging, Thompson<sup>35</sup> et al and Richey<sup>31</sup> et al stratified recovery trajectory by age group and Roy<sup>44</sup> et al compared recovery with and without depressive symptoms. One study, Chiang<sup>22</sup> et al, was able to identify worse recovery trajectories in a group of patients with a high early symptom burden in a small cohort of patients. Overall, the limited exploration of factors affecting recovery trajectory reported in the included studies prevents identification of different recovery trajectories being characterised for different patient subgroups.

*Comparison to previous literature*

As highlighted by Voormolen et al, measures of prevalence of post-concussion symptoms and functional outcomes can vary widely when different classification methods are used.<sup>49</sup> Our review found considerable variation in the prevalence of impairment estimated at the same time points both with the same outcome measures and with different measures. Using the RPQ up to 52% of patients were estimated to have one or more new post-concussion symptom at 3 and 6-months,<sup>21,23</sup> with mean 3 and 6 month RPQ scores varying 10 fold between studies (with different inclusion criteria and subgroups). Mean scores RPQ scores in 7 cohorts with 12 month follow up varied three fold with the range of mean scores encompassing that recorded by other large studies.<sup>50</sup> An estimated 29% to 64% of patients had a GOSE< 8 at 3 months and 21% to 65.4% at 6 months.<sup>27,31</sup>

Our review found a similar prevalence of post-concussion symptoms following mTBI to that reported by Cancelliere et al (31.3%) at 3 to 6 months post injury.<sup>5</sup> As in previous studies, our review found CT findings and pre-morbid psychiatric history to be predictors of worse recovery.<sup>8,15,16</sup> However, our systematic review is unique in identifying the trajectory of recovery after 3-months of injury across a diverse range of outcome measures. The only other review which assessed trajectory of recovery focused on the period immediately following injury to 4-6 weeks post injury.<sup>14</sup> Although not the

primary focus of our review, we found a similar magnitude of recovery to McCrae et al<sup>14</sup> during this early period.

### Implications

When clinically assessing patients with persistent impairment at 3-months following mild and moderate TBI it is important to be able to advise them of their likely recovery trajectory. Our review highlights that symptoms and impairments at 3 months, as measured using RPQ, GOSE, SF-36 and QOLIBRI, are likely to persist -at 6 to 12 months. However, there is limited evidence to identify which patients are likely to have such persistent symptoms, and it seems possible that at 3 months symptom free patients could subsequently deteriorate given the findings of this review. Research like that conducted by Chiang et al<sup>22</sup> aimed at identifying patient subgroups based on early symptom burden with different recovery trajectories in the first year following TBI is needed to provide patients with individualised advice regarding their prognosis.

Moreover, the prevalence of patients who have persisting impairment at 3-months and later time points varied widely based on different analyses of the RPQ (mean, median scores/numbers of symptoms and percentages with number of symptoms above varying cut off)<sup>47</sup> and differing summaries of other outcome measures used. Although efforts are being made to ensure common data elements are collected in TBI studies, there is a need to standardise which outcomes are used to assess symptom burden and thresholds used to identify persisting post-concussion symptoms.<sup>11</sup> Differences in reporting between studies even using the same outcome measure prevented meta-analysis. The need to be able to provide patients with individualised prognoses following TBI and measure outcomes that best reflect the impact of TBI on patients are research priorities identified in the James Lind Alliance research priority setting exercise for concussion.<sup>51</sup> Future research needs to address this challenge whilst minimising post TBI losses to follow up.<sup>52</sup> The heterogeneity identified in 3-12 month outcomes of so called mild TBI speaks to the need for a more nuanced multidimensional disease characterisation that may provide more clarity in providing patients with prognosis. To this end a recent proposal recommends -moving away from the mild/moderate dichotomisation of TBI -to a more granular assessment based on the initial GCS score (e.g., 13,14).<sup>52-54,54</sup>

### Conclusion

A significant proportion of patients were found to have symptoms or impairment following mild and moderate TBI across different studies at 3-months following injury. Most of these patients had persisting impairment at 6- and 12-months following injury. There was limited evidence available to identify factors which affect the recovery trajectory, and frequent exclusion of vulnerable subgroups. Studies were heterogenous in inclusion criteria, reported multiple outcome measures and used different thresholds to classify persisting symptoms, which led to wide variation in estimates of symptom burden. Standardised reporting of outcome measures is needed as part of common data elements to enable future research to identify factors predicting the outcome trajectory at 3at 3 months after TBI.

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**Author contributions**

AM, LW and FL conceived the study and approved part funding from CENTER TBI Work Package 17. CM, FL, RW, AP and LW developed the review protocol subsequently published on PROSPERO; taking account of TBI lived experience (JP), specialist neurorehabilitation (RS) and wider emergency care (TS, MT) perspectives.

AP and RW developed the database search strategies and conducted the electronic searches, importing citations into the review reference software. CM, MT and TL independently screened citation title and abstracts for relevance. CM, MT, TL and FL independently assessed full texts of studies potentially meeting the inclusion criteria, extracting outcome data and conducting quality assessments of included studies.

CM and FL tabulated the reported outcomes from included studies, conducted a narrative synthesis of outcomes and drafted the manuscript. All authors reviewed and provided comments on the manuscript and approved the final draft for submission.

**Conflict of interest** We have no conflicts of interest to declare

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**Transparency and Reproducibility statement**

We conducted this systematic review according to the protocol published on PROSPERO from <https://www.crd.york.ac.uk/PROSPERO/view/CRD42021264931>. The search strategies and results are summarised in the main text PRISMA diagram and tables in the manuscript with further detail (search strategies and data extraction tables) in the supplementary material and list of citations plus excluded studies.

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Table 1: Quality assessment of included studies

| Study                              | Overall score | Rating * |
|------------------------------------|---------------|----------|
| Al Fauzi et al <sup>18</sup>       | 15            | Fair     |
| Candrian et al <sup>19</sup>       | 13            | Poor     |
| Carroll et al <sup>20</sup>        | 12            | Poor     |
| Chakroun et al <sup>21</sup>       | 12            | Poor     |
| Chiang et al <sup>22</sup>         | 12            | Poor     |
| Heitger et al <sup>23,24,39</sup>  | 10,10,14      | Poor     |
| Karaliute et al <sup>25</sup>      | 12            | Poor     |
| Kraus et al <sup>26</sup>          | 13            | Poor     |
| Madhok et al <sup>27</sup>         | 13            | Poor     |
| McCrea et al <sup>28</sup>         | 15            | Fair     |
| McMahon et al <sup>29</sup>        | 15            | Fair     |
| Nelson et al <sup>30</sup>         | 16            | Fair     |
| Richey et al <sup>31</sup>         | 14            | Poor     |
| Roe et al <sup>32</sup>            | 10            | Poor     |
| Sandhaug et al <sup>33</sup>       | 10            | Poor     |
| Sigurdardottir et al <sup>34</sup> | 9             | Poor     |
| Thompson et al <sup>35</sup>       | 9             | Poor     |
| Voormolen et al <sup>37</sup>      | 17            | Fair     |
| Verberne et al <sup>36</sup>       | 13            | Poor     |
| Yue et al <sup>38</sup>            | 16            | Fair     |
| Machamer et al <sup>40</sup>       | 18            | Fair     |
| Keatley et al <sup>41</sup>        | 16            | Fair     |
| Hume et al <sup>42</sup>           | 15            | Fair     |
| Norrie et al <sup>43</sup>         | 13            | Poor     |
| Roy et al <sup>44</sup>            | 13            | Poor     |
| Martha et al <sup>45</sup>         | 13            | Poor     |
| Miller et al <sup>46</sup>         | 13            | Poor     |
| Thuss et al <sup>47</sup>          | 19            | Fair     |

\* Methodological quality was classified as “excellent” if studies had a score of 26 or higher, “good” if scores ranged between 20 and 25, “fair” if they ranged between 15 and 19, and “poor” if the score was 14 or lower.<sup>17</sup>

Table 2: Outcomes assessed

| Outcome assessed                                               | Number of studies | Total patients |
|----------------------------------------------------------------|-------------------|----------------|
| Rivermead Post concussion Symptoms Questionnaire               | 15                | 5,570          |
| Glasgow Outcome Scale                                          | 13                | 4,155*         |
| Short Form-36 Health Survey                                    | 5                 | 1,433          |
| Quality of after Life Brain Injury                             | 3                 | 1,265          |
| Functional Independence Measure/ Functional Status Examination | 2                 | 74             |
| Check list of Post concussion symptoms                         | 1                 | 100            |
| Barthel Index                                                  | 1                 | 16             |
| EuroQol 5 Dimension 5 Level Survey                             | 1                 | 182            |
| Acute Concussion Evaluation                                    | 1                 | 260            |
| World Health Organisation Quality of Life Scale                | 1                 | 40             |
| Depression, anxiety and stress scale                           | 1                 | 40             |
| Fatigue Severity Scale                                         | 1                 | 159            |

\*3624 unique patients after accounting for overlap of TRACK TBI cohorts<sup>27,29,38</sup>

Table 3: Studies reporting outcomes for the Rivermead Post concussion Symptoms Questionnaire

| Study                                                        | Total Patient<br>s | Discharge/early outcome                                                                                                       | 3 Months                                                                                                                     | 6 Months                                                                                                                      | 1 Year                                                                                                                     | 2 Years                                       |
|--------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| Candrian et al <sup>19</sup>                                 | 35                 | Mean score 15.51 SD 8                                                                                                         | Mean 8.97 SD 10.6                                                                                                            |                                                                                                                               | Mean 6.69 SD 9.5                                                                                                           |                                               |
| Carroll et al <sup>20</sup>                                  | 61                 | Mean score 14<br>32% > 2 new post injury symptoms                                                                             | Mean 10.8<br>28% > 2 new post injury symptoms                                                                                | Mean 10.8<br>23% > 2 new post injury symptoms                                                                                 | Mean 10.8<br>18 % > 2 new post injury symptoms                                                                             | Mean 10.9<br>22% > 2 new post injury symptoms |
| Chakroun-Walha et al <sup>21</sup>                           | 130                | 54.6% > 3 new post injury symptoms                                                                                            | N=91 22% > 3 new post injury symptoms                                                                                        | N=56 21.4% > 3 new post injury symptoms                                                                                       |                                                                                                                            |                                               |
| Heitger et al <sup>23,24</sup><br>(3 papers same population) | 37                 | Mean 19.81 (SD11.72)<br>91% Any new post injury symptom                                                                       | Mean 9.81 (SD9.89)<br>59% Any new post injury symptom                                                                        | Mean 10.24 SD (10.65)<br>52% Any new post injury symptom                                                                      | Mean 10.13 SD 11.9<br>51% Any new post injury symptom                                                                      |                                               |
| Karaliute et al <sup>25</sup>                                | 318                | 50% 159/318 symptoms<br>Mean 6.4 SD 10.9                                                                                      | 25.5% 83/326 symptoms<br>Mean 9.8 SD 10.9                                                                                    |                                                                                                                               | 19.1% 54/282 symptoms<br>Mean 5.1 SD 8.1                                                                                   |                                               |
| Kraus et al <sup>26</sup>                                    | 2005               |                                                                                                                               | Mean 7.3                                                                                                                     | Mean 3.6                                                                                                                      |                                                                                                                            |                                               |
| Richey et al <sup>31</sup>                                   | 447                | >1 symptom<br>132/259 (51%) <65<br>11/74 (14.9%) 65+                                                                          | >1 symptom<br>120/239 (50.2%) <65<br>24/66 (36.4%) 65+                                                                       | >1 symptom<br>107/221 (48.4%) <65<br>11/59 (18.6%) 65+                                                                        |                                                                                                                            |                                               |
| Roe et al <sup>32</sup>                                      | 52                 |                                                                                                                               | Any new symptom 38 (73%)                                                                                                     | Any new symptom 26 (50%)                                                                                                      | Any new symptom 22 (42%)                                                                                                   |                                               |
| Sigurdardottir et al <sup>27</sup>                           | 74                 |                                                                                                                               | mTBI=40 Mean 20.8 (SD18.3)<br>Moderate TBI=34 Mean 17 (15.4)                                                                 |                                                                                                                               | mTBI=33 Mean 15.9 (16.9)<br>Moderate TB=33 Mean 15.6 (16.2)                                                                |                                               |
| Machamer et al <sup>40</sup>                                 | 1593               | N 1593<br>Mean 18.4 SD (14.9)<br>Median 15 IQR (6, 28)<br><br>Number of symptoms:<br>Mean 6.8 SD (4.8)<br>Median 6 IQR (3,11) | N 1480<br>Mean 14.2 SD (14.8)<br>Median 9 IQR (3, 11)<br><br>Number of symptoms:<br>Mean 5.2 SD (4.9)<br>Median 4 IQR (1, 9) | N 1397<br>Mean 12.9 SD (14.6)<br>Median 8 IQR (0, 20.5)<br><br>Number of symptoms:<br>Mean 4.9 SD (4.9)<br>Median 3 IQR (0,8) | N 1292<br>Mean 12.2 SD (14.2)<br>Median 6 IQR (0,20)<br><br>Number of symptoms:<br>Mean 4.6 SD (4.8)<br>Median 3 IQR (0,8) |                                               |
| Keatley et al <sup>41</sup>                                  | 253                | Mean 14.2 SD 10.04                                                                                                            | Mean 12.34 SD 12.59                                                                                                          | Mean 11.01SD 12.91                                                                                                            |                                                                                                                            |                                               |

|                            |     |                                                                                         |                                                                                           |                                                                                         |  |  |
|----------------------------|-----|-----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|--|--|
| Norrie et al <sup>43</sup> | 159 | Fatigue item mean 2.09 (SD 1.24)                                                        | Fatigue item mean 1.03 (SD1.05)                                                           | Fatigue item mean 0.96 (SD1.05)                                                         |  |  |
| Roy et al <sup>44</sup>    | 217 | 217<br>169 no depressive symptoms<br>48 depressive symptoms                             | No depressive symptoms<br>Mean 8.2 SD (8.7)<br>Depressive Symptoms<br>Mean 30.7 SD (15.2) | No depressive symptoms<br>Mean 6.3 SD (8)<br>Depressive Symptoms<br>Mean 32.3 SD (14.6) |  |  |
| Martha et al <sup>45</sup> | 18  | 11 older adults (55 and over)<br>Mean 25.1 ± 8.1<br>7 younger adults<br>Mean 21.4 ± 9.1 | 11 older adults (55 and over)<br>Mean 18.0 ± 7.1<br>7 younger adults<br>Mean 14.6 ± 4.8   | 11 older adults (55 and over)<br>Mean 17.1 ± 3.6<br>7 younger adults<br>Mean 12.6 ± 3.5 |  |  |
| Miller et al <sup>46</sup> | 171 | Mean 17.96 (SD 13.40)                                                                   | Mean 11.73 (SD 15.75)                                                                     | Mean 10.68 (SD 14.48)                                                                   |  |  |

Table 4: Studies reporting outcomes for the Glasgow Outcome Scale Extended (GOSE)

| Study                         | Total Patients                                                                                | Discharge/early outcome                                           | 3 Months                                                     | 6 Months                                                           | 1 Year                                             | 2 Years                |
|-------------------------------|-----------------------------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------------|----------------------------------------------------|------------------------|
| Al Fauzi et al <sup>18</sup>  | 32<br>16 control<br>16 intervention                                                           | Control<br>Mean 2.5* (SD 0.5)<br>Intervention<br>Mean 3* (SD 0.5) | Control<br>Mean 3*(SD 0)<br>Intervention<br>Mean 3* (SD 0.4) | Control<br>Mean 3.5* (SD 0.5)<br>Intervention<br>Mean 3.5 *(S 0.5) |                                                    |                        |
| Carroll et al <sup>20</sup>   | 61                                                                                            |                                                                   | Mean 7.3<br>25% GOSE <8                                      | Mean 7.5<br>30% GOSE<8                                             | Mean 7.4<br>29% GOSE<8                             | Mean 7.4<br>28% GOSE<8 |
| Chiang et al <sup>22</sup>    | 100<br>18 Moderate recovery (initial GOSE mean <7)<br>82 Fine recovery (initial GOSE mean ≥7) | Mean<br>Moderate Recovery 6.8<br>Fine Recovery 7.6                | Mean<br>Moderate Recovery 7<br>Fine Recovery 8               |                                                                    | Mean<br>Moderate Recovery 7.7<br>Fine Recovery 8   |                        |
| Madhok et al <sup>27</sup>    | 271 total                                                                                     |                                                                   | N=211 GOSE <8<br>127/211 (60.2%)                             | N=185 GOSE <8<br>121/185 (65.4%)                                   |                                                    |                        |
| McCrea et al <sup>28</sup>    | 93 moderate TBI                                                                               | 41% GOSE >3                                                       | N=84<br>69% GOSE >3                                          | N=75<br>71% GOSE>3                                                 | N=72<br>75% GOSE>3                                 |                        |
| McMahon et al <sup>29</sup>   | 348                                                                                           |                                                                   | N=348<br>Mean 6.9 (SD1.1)                                    | N=305<br>Mean 6.9 (SD 1.0)                                         | N=199<br>Mean 7.1 (SD 1.0)                         |                        |
| Nelson et al <sup>30</sup>    | 1154                                                                                          | N=975 87% GOSE <8                                                 | 64% GOSE <8                                                  | 60% GOSE <8                                                        | N=768 53% GOSE <8                                  |                        |
| Richey et al <sup>31</sup>    | 447                                                                                           | GOSE<8<br>Age <65<br>160/258 (65.1%)<br>Age 65+ 26/76 (34.2%)     | GOSE<8<br>Age <65<br>146/240 (60.8%)<br>Age 65+ 20/69 (29%)  | GOSE<8<br>Age <65<br>131/225 (58.2%)<br>Age 65+ 14/66 (21.2%)      |                                                    |                        |
| Sandhaug et al <sup>33</sup>  | 20                                                                                            |                                                                   | Mean 5 SD 1                                                  |                                                                    | Mean 6 SD 2                                        | Mean 6 SD 2            |
| Thompson et al <sup>35</sup>  | 33 Younger<br>Older age group<br>65+(n=15)                                                    |                                                                   | Younger<br>Mean 6.9 SD 1.4<br>Older Mean 5.1 SD 2.3          | Younger<br>Mean 7.3 SD 1.4<br>Older Mean 5.2 SD 2.4                | Younger<br>Mean 7.3 SD 1.5<br>Older Mean 4.6 SD .1 |                        |
| Voormolen et al <sup>37</sup> | 1104                                                                                          |                                                                   | Uncomplicated mTBI<br>GOSE<7 23%<br>Mean 7.2 SD 1.1          | Uncomplicated<br>mTBI GOSE<7 16%<br>Mean 7.3SD 1.1                 |                                                    |                        |

|                           |     |  |                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                      |  |  |
|---------------------------|-----|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|
|                           |     |  | Complicated mTBI<br>GOSE<7 41%<br>Mean 6.5 SD 1.4                                                                                                                                                                                                                                                              | Complicated mTBI<br>GOSE<7 35%<br>Mean 6.7 SD 1.3                                                                                                                                    |  |  |
| Yue et al <sup>38</sup>   | 260 |  | GOSE<7<br>80 (30.8%)                                                                                                                                                                                                                                                                                           | GOSE<7<br>80 (30.8%)                                                                                                                                                                 |  |  |
| Roy et al <sup>44</sup>   | 217 |  | GOSE=8<br>No Depressive<br>symptoms<br>84 (49.4%)<br>Depressive symptoms<br>1 (3.2%)                                                                                                                                                                                                                           | N=181 GOSE=8<br>No Depressive<br>symptoms<br>89 (60.1%)<br>Depressive<br>symptoms<br>2 (6.9%)                                                                                        |  |  |
| Thuss et al <sup>47</sup> | 154 |  | GOSE<8<br>89 (58%)<br>Predicted by baseline<br>factors of living situation,<br>intracranial injury HADS -D<br>(hospital anxiety and<br>depression scale) and HISC<br>(head injury symptoms<br>checklist) at baseline in mv<br>model of demographic,<br>comorbid and injury<br>factors in multivariate<br>model | GOSE<8<br>69 (47%)<br><br>No significant<br>predictors in<br>multivariate model<br><br>28 of 89 with 3 month<br>GOSE<8 improved<br><br>11 of 66 with 3 month<br>GOSE =8 deteriorated |  |  |

\*Out of maximum 5 on Glasgow Outcome Scale (not Extended Glasgow Outcome Scale where range is 1-8 with the additional differentiation of upper and lower levels for GOS 3-5)

Table 5: Studies reporting outcomes for Short Form-36 Health Survey

| Study                        | Total Patients                   | Discharge/early outcome                                                                                                                                                                                                                                                                   | 3 Months                                                                                                                                                                                                                                                                                  | 6 Months                                                                                                                                         | 1 Year                                                                                                                                                                                                                                                                                   |
|------------------------------|----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Chiang et al <sup>22</sup>   | 100                              | <p>PCS</p> <p>Under average QoL and worsening (n=14) Mean =40</p> <p>Under average QoL and improving (n=35) Mean =40</p> <p>Fine QoL and slight worsening (n=51) Mean=59</p> <p>MCS</p> <p>Persistently under average QOL (n=11) Mean =33</p> <p>Persistently fine QOL (n=89) Mean=52</p> | <p>PCS</p> <p>Under average QoL and worsening (n=14) Mean = 39</p> <p>Under average QoL and improving (n=35) Mean=42</p> <p>Fine QoL and slight worsening (n=51) Mean=59</p> <p>MCS</p> <p>Persistently under average QOL (n=11) Mean =32</p> <p>Persistently fine QOL (n=89) Mean=52</p> |                                                                                                                                                  | <p>PCS</p> <p>Under average QoL and worsening (n=14) Mean =32</p> <p>Under average QoL and improving (n=35) Mean=49</p> <p>Fine QoL and slight worsening (n=51) Mean=58</p> <p>MCS</p> <p>Persistently under average QOL (n=11) Mean =31</p> <p>Persistently fine QOL (n=89) Mean=52</p> |
| Heitger et al <sup>39</sup>  | 37                               | <p>PCS Mean 44</p> <p>MCS Mean 43</p>                                                                                                                                                                                                                                                     | <p>PCS Mean 56</p> <p>MCS Mean 49</p>                                                                                                                                                                                                                                                     | <p>PCS Mean 56</p> <p>MCS Mean 51</p>                                                                                                            |                                                                                                                                                                                                                                                                                          |
|                              | 37 controls                      | <p>PCS Mean 58</p> <p>MCS 55</p>                                                                                                                                                                                                                                                          | <p>PCS Mean 58</p> <p>MCS Mean 55</p>                                                                                                                                                                                                                                                     | <p>PCS Mean 58</p> <p>MCS Mean 55</p>                                                                                                            |                                                                                                                                                                                                                                                                                          |
| Thompson et al <sup>35</sup> | 33<br>Older age group 65+ (n=15) | <p>PCS</p> <p>Younger Mean 43.6 SD 12.2</p> <p>Older Mean 34 SD 15.2</p> <p>MCS</p> <p>Younger Mean 47.6 SD 10.1</p> <p>Older Mean 47.1 SD 15.1</p>                                                                                                                                       | <p>PCS</p> <p>Younger Mean 41.7 SD 10.1</p> <p>Older Mean 32.8 SD 9.3</p> <p>MCS</p> <p>Younger Mean 48.8 SD 6.5</p> <p>Older Means 51.8 SD 9.7</p>                                                                                                                                       | <p>PCS</p> <p>Younger Mean 51.1 SD 9.2</p> <p>Older Mean 36.3 SD 10.9</p> <p>MCS</p> <p>Younger Mean 49.9 SD 6.5</p> <p>Older Mean 55 SD 7.2</p> | <p>PCS</p> <p>Younger Mean 50.5 SD 11.7</p> <p>Older Mean 33.3 SD 9.7</p> <p>MCS</p> <p>Younger Mean 49.1 SD 7</p> <p>Older Mean 56 SD 9.3</p>                                                                                                                                           |

|                               |      |                                    |                                                                                                                                                                                              |                                                                                                                                                                                            |  |
|-------------------------------|------|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|                               |      |                                    |                                                                                                                                                                                              |                                                                                                                                                                                            |  |
| Voormolen et al <sup>37</sup> | 1104 |                                    | Uncomplicated mTBI<br>PCS <40 =24%<br>Mean 47.4 SD 10.6<br>MCS <40= 22%<br>Mean 48.2 SD 10.9<br><br>Complicated mTBI<br>PCS <40 =29%<br>Mean 45.6 SD 10.2<br>MCS <40 =30%<br>Mean 46 SD 12.1 | Uncomplicated mTBI<br>PCS <40 =21%<br>Mean 48.6 SD 10.4<br>MCS <40 =21%<br>Mean 48.6 SD 11.1<br><br>Complicated mTBI<br>PCS <40 =22%<br>Mean 47.6 SD 10<br>MCS<40 = 28%<br>Mean 47.2 SD 12 |  |
| Norrie et al <sup>43</sup>    | 159  | SF36 Vitality<br>Mean 46.6 SD 24.7 | SF 36 Vitality<br>Mean 60.2 SD 19.7                                                                                                                                                          | SF 36 Vitality<br>Mean 62.1 SD 20.2                                                                                                                                                        |  |

Table 5 Abbreviation key: PCS= SF36 Physical component summary, MCS = SF36 Mental component summary, QOL=Quality of life, SD=Standard Deviation

Table 6: Studies reporting outcomes for Quality of Life Brain after Injury Scale

| Study                         | Total Patients                                      | Discharge/early outcome                  | 3 Months                                                                                                 | 6 Months                                                                                                | 1 Year                                   | 2 Years |
|-------------------------------|-----------------------------------------------------|------------------------------------------|----------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|------------------------------------------|---------|
| Carroll et al <sup>20</sup>   | 61                                                  | Mean=75                                  | Mean=80                                                                                                  | Mean=80                                                                                                 | Mean=81                                  | Mean=82 |
| Chiang et al <sup>22</sup>    | 100<br>41 poor QOL baseline<br>59 fine QOL baseline | Poor<br>Mean 2.3<br><br>Fine<br>Mean 3.5 | Poor<br>Mean 2.5<br><br>Fine<br>Mean 3.5                                                                 |                                                                                                         | Poor<br>Mean 3.5<br><br>Fine<br>Mean 3.7 |         |
| Voormolen et al <sup>37</sup> | 1104                                                |                                          | Uncomplicated mTBI<br><60 =19%<br>Mean 74.8 SD 16.5<br>Complicated mTBI<br><60 = 26%<br>Mean 70.8SD 17.5 | Uncomplicated mTBI<br><60 = 19%<br>Mean 75.2SD 17.2<br>Complicated mTBI<br><60 =21%<br>Mean 72.3SD 17.2 |                                          |         |

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Table 7 Factors assessed for impact on outcomes at or later than 3 months post sustaining moderate or mild TBI

| Risk factor                                        | Number of studies                        | Number of studies assessing effect of variable on outcome trajectory or at single/ multiple time points |                                   |                             | Studies predictive of outcome multiple time points |
|----------------------------------------------------|------------------------------------------|---------------------------------------------------------------------------------------------------------|-----------------------------------|-----------------------------|----------------------------------------------------|
|                                                    |                                          | Randomised allocation                                                                                   | Univariable Analysis (N)          | Multivariable analysis (N)  |                                                    |
| Age                                                | 10 <sup>22,24,27,31,35,38,41,45-47</sup> |                                                                                                         | 8 <sup>22,27,31,35,41,45-47</sup> | 4 <sup>22,24,38,46</sup>    | 4 <sup>22,35,45,46</sup>                           |
| Sex                                                | 7 <sup>22,27,32,38,41,46,47</sup>        |                                                                                                         | 6 <sup>22,27,32,41,46,47</sup>    | 3 <sup>38,46,47</sup>       | 3 <sup>41,46,47</sup>                              |
| Educational attainment/years in Education          | 7 <sup>22,24,27,38,41,46,47</sup>        |                                                                                                         | 5 <sup>22,27,41,46,47</sup>       | 5 <sup>22,24,27,38,46</sup> | 1 <sup>22,27,41,46*</sup>                          |
| Initial GCS                                        | 5 <sup>24,27,38,46,47</sup>              |                                                                                                         | 4 <sup>27,38,46,47</sup>          | 3 <sup>24,38,46</sup>       | 1 <sup>46</sup>                                    |
| CT findings                                        | 5 <sup>29,30,37,38,47</sup>              |                                                                                                         | 4 <sup>29,30,37,47</sup>          | 2 <sup>38,47</sup>          | 2 <sup>30,37*</sup>                                |
| Psych disease                                      | 4 <sup>27,38,41,47</sup>                 |                                                                                                         | 3 <sup>27,41,47</sup>             | 2 <sup>27,38</sup>          | 3 <sup>27,38,41</sup>                              |
| LOC                                                | 3 <sup>27,41,46</sup>                    |                                                                                                         | 3 <sup>27,41,46</sup>             | 1 <sup>46</sup>             | 1 <sup>41,46</sup>                                 |
| Post traumatic amnesia                             | 3 <sup>27,41,46</sup>                    |                                                                                                         | 1 <sup>27,41,46</sup>             | 1 <sup>46</sup>             | 1 <sup>46</sup>                                    |
| Intoxicated when injured                           | 3 <sup>27,32,41</sup>                    |                                                                                                         | 3 <sup>27,32,41</sup>             |                             |                                                    |
| Race                                               | 3 <sup>27,41,46</sup>                    |                                                                                                         | 3 <sup>27,41,46</sup>             | 2 <sup>27,46</sup>          | 3 <sup>27,41,46</sup>                              |
| Ethnicity                                          | 2 <sup>27,46</sup>                       |                                                                                                         | 2 <sup>27,46</sup>                | 2 <sup>27,46</sup>          | 1 <sup>27</sup>                                    |
| Living alone                                       | 2 <sup>32,47</sup>                       |                                                                                                         | 2 <sup>32,47</sup>                |                             |                                                    |
| Married/partnered                                  | 2 <sup>22,41</sup>                       |                                                                                                         | 2 <sup>22,41</sup>                |                             |                                                    |
| Employment                                         | 2 <sup>22,41</sup>                       |                                                                                                         | 2 <sup>22,41</sup>                | 1 <sup>22</sup>             | 1 <sup>22*</sup>                                   |
| Injury Mechanism                                   | 2 <sup>27,46</sup>                       |                                                                                                         | 2 <sup>27,46</sup>                | 2 <sup>27,46</sup>          | 2 <sup>27,46</sup>                                 |
| Had CT imaging                                     | 1 <sup>46</sup>                          |                                                                                                         | 1 <sup>46</sup>                   | 1 <sup>46</sup>             | 1 <sup>46</sup>                                    |
| Anti-coagulant                                     | 1 <sup>27</sup>                          |                                                                                                         | 1 <sup>27</sup>                   |                             |                                                    |
| Cardiovascular disease                             | 1 <sup>38</sup>                          |                                                                                                         |                                   | 1 <sup>38</sup>             |                                                    |
| GI disease                                         | 1 <sup>38</sup>                          |                                                                                                         |                                   | 1 <sup>38</sup>             |                                                    |
| Resp disease                                       | 1 <sup>38</sup>                          |                                                                                                         |                                   | 1 <sup>38</sup>             |                                                    |
| Comorbidities                                      | 1 <sup>22,47</sup>                       |                                                                                                         | 1 <sup>22,47</sup>                |                             |                                                    |
| Headache/migraine                                  | 1 <sup>38</sup>                          |                                                                                                         |                                   | 1 <sup>38</sup>             | 1 <sup>38</sup>                                    |
| Prior concussions                                  | 1 <sup>41</sup>                          |                                                                                                         | 1 <sup>41</sup>                   |                             |                                                    |
| Work related injury                                | 1 <sup>41</sup>                          |                                                                                                         | 1 <sup>41</sup>                   |                             |                                                    |
| Altered mental state                               | 1 <sup>41</sup>                          |                                                                                                         | 1 <sup>41</sup>                   |                             |                                                    |
| Toxicology screen                                  | 1 <sup>27</sup>                          |                                                                                                         | 1 <sup>27</sup>                   | 1 <sup>27</sup>             |                                                    |
| Hypotension                                        | 1 <sup>27</sup>                          |                                                                                                         | 1 <sup>27</sup>                   |                             |                                                    |
| Hypoxia                                            | 1 <sup>27</sup>                          |                                                                                                         | 1 <sup>27</sup>                   |                             |                                                    |
| AIS                                                | 1 <sup>32</sup>                          |                                                                                                         | 1 <sup>32</sup>                   |                             |                                                    |
| Household income                                   | 1 <sup>22,46</sup>                       |                                                                                                         | 2 <sup>22,46</sup>                | 1 <sup>46</sup>             | 1 <sup>46</sup>                                    |
| Deprivation index                                  | 1 <sup>46</sup>                          |                                                                                                         | 1 <sup>46</sup>                   | 1 <sup>46</sup>             | 1 <sup>46</sup>                                    |
| Health Insurance                                   | 1 <sup>46</sup>                          |                                                                                                         | 1 <sup>46</sup>                   | 1 <sup>46</sup>             | 1 <sup>46</sup>                                    |
| Injury related litigation                          | 1 <sup>46</sup>                          |                                                                                                         | 1 <sup>46</sup>                   | 1 <sup>46</sup>             | 1 <sup>46</sup>                                    |
| Early motor function (eye movement + arm function) | 1 <sup>23</sup>                          |                                                                                                         |                                   | 1 <sup>23</sup>             | 1 <sup>23</sup>                                    |
| IC P3NOGO amplitudes                               | 1 <sup>19</sup>                          |                                                                                                         | 1 <sup>19</sup>                   |                             | 1 <sup>19</sup>                                    |

**Figure legend**

Figure 1: PRISMA Diagram

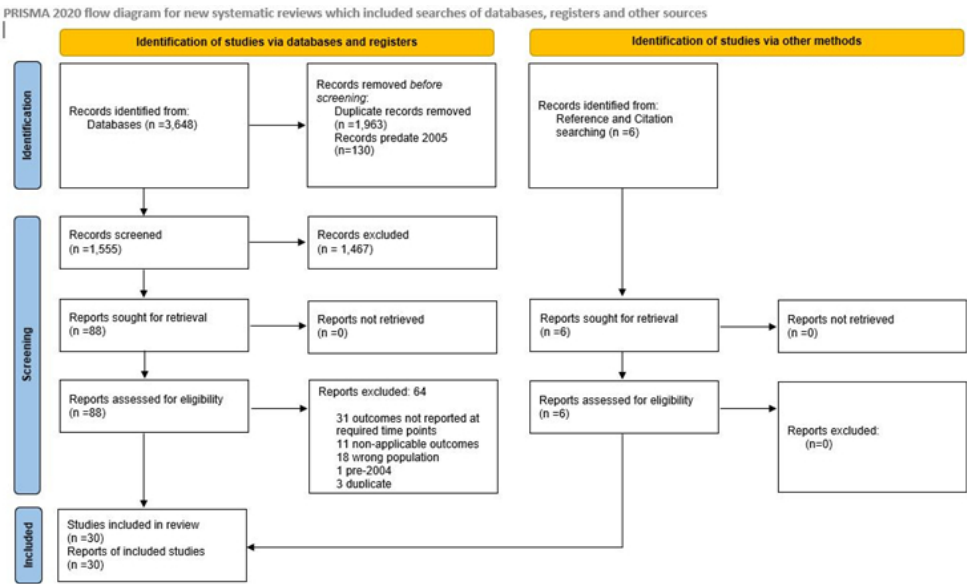


Figure 1 PRISMA diagram

159x95mm (120 x 120 DPI)

## Supplementary Material 1: Database search strategies

## Summary table

| Database                                                                                    | Dates covered   | Results since 2005 |
|---------------------------------------------------------------------------------------------|-----------------|--------------------|
| MEDLINE(R) ALL (Ovid)                                                                       | 1946 to Present | 994                |
| EMBASE (Ovid)                                                                               | 1974 to Present | 1557               |
| CINAHL (EBSCO)                                                                              | 1974 to Present | 316                |
| Science Citation Index Expanded, Conference Proceedings Citation Index- Science (Clarivate) | 1900 to Present | 781                |
| Total retrieved                                                                             | -               | 3648               |
| Unique records in database                                                                  | -               | 1555               |

## Full search strategies

Ovid MEDLINE(R) ALL 1946 to May 20, 2025  
21<sup>st</sup> May 2025

| #  | Searches                                                                                                                                                             |  |
|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| 1  | *craniocerebral trauma/ or exp *brain injuries/                                                                                                                      |  |
| 2  | ((head or brain) adj3 (injur* or trauma)).ti,ab.                                                                                                                     |  |
| 3  | or/1-2                                                                                                                                                               |  |
| 4  | (mild or moderate).mp.                                                                                                                                               |  |
| 5  | cohort studies/                                                                                                                                                      |  |
| 6  | longitudinal studies/                                                                                                                                                |  |
| 7  | follow-up studies/                                                                                                                                                   |  |
| 8  | prospective studies/                                                                                                                                                 |  |
| 9  | retrospective studies/                                                                                                                                               |  |
| 10 | (cohort* or longitudinal or prospective or retrospective or follow-up or "follow up" or cross-section* or "cross section*" or "post-injur*" or "post injur*").ti,ab. |  |
| 11 | 3 and 4 and (5 or 6 or 7 or 8 or 9 or 10)                                                                                                                            |  |
| 12 | ("glasgow outcome scale" or gos).ti,ab.                                                                                                                              |  |
| 13 | ("extended glasgow outcome scale" or gos-e or gose).ti,ab.                                                                                                           |  |
| 14 | ("rivermead post concussion symptoms questionnaire" or rpq).ti,ab.                                                                                                   |  |
| 15 | (euro qual or euro qual5d or euro qol5d or eq-5d or eq5-d or eq5d or euroqual or euroqol or euroqual5d or euroqol5d).ti,ab.                                          |  |

|    |                                                             |  |
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| 16 | ("quality of life after brain injury" or qolibri).ti,ab.    |  |
| 17 | (sf12 or "sf 12" or sf twelve or sftwelve).ti,ab.           |  |
| 18 | (sf36* or "sf 36*" or sf thirtysix or sf thirty six).ti,ab. |  |
| 19 | or/12-18                                                    |  |
| 20 | 11 and 19                                                   |  |
|    |                                                             |  |

**Embase 1974 to 2025 Week 20**  
**21<sup>st</sup> May 2025**

| #  | Searches                                                                                                                                                             |  |
|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| 1  | *head injury/ or exp *brain injury/                                                                                                                                  |  |
| 2  | ((head or brain) adj3 (injur* or trauma)).ti,ab.                                                                                                                     |  |
| 3  | or/1-2                                                                                                                                                               |  |
| 4  | (mild or moderate).mp.                                                                                                                                               |  |
| 5  | exp cohort analysis/                                                                                                                                                 |  |
| 6  | exp longitudinal study/                                                                                                                                              |  |
| 7  | exp follow up/                                                                                                                                                       |  |
| 8  | exp prospective study/                                                                                                                                               |  |
| 9  | retrospective study/                                                                                                                                                 |  |
| 10 | (cohort* or longitudinal or prospective or retrospective or follow-up or "follow up" or cross-section* or "cross section*" or "post-injur*" or "post injur*").ti,ab. |  |
| 11 | 3 and 4 and (5 or 6 or 7 or 8 or 9 or 10)                                                                                                                            |  |
| 12 | ("extended glasgow outcome scale" or gos-e or gose).ti,ab.                                                                                                           |  |
| 13 | ("glasgow outcome scale" or gos).ti,ab.                                                                                                                              |  |
| 14 | ("rivermead post concussion symptoms questionnaire" or rpq).ti,ab.                                                                                                   |  |
| 15 | (euro qual or euro qual5d or euro qol5d or eq-5d or eq5-d or eq5d or euroqual or euroqol or euroqual5d or euroqol5d).ti,ab.                                          |  |
| 16 | ("quality of life after brain injury" or qolibri).ti,ab.                                                                                                             |  |
| 17 | (sf12 or "sf 12" or sf twelve or sftwelve).ti,ab.                                                                                                                    |  |
| 18 | (sf36* or "sf 36*" or sf thirtysix or sf thirty six).ti,ab.                                                                                                          |  |
| 19 | or/12-18                                                                                                                                                             |  |
| 20 | 11 and 19                                                                                                                                                            |  |
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**CINAHL**  
**22<sup>nd</sup> May 2025**

| #  | Searches                                                                                         |  |
|----|--------------------------------------------------------------------------------------------------|--|
| S1 | (MM "Head Injuries")                                                                             |  |
| S2 | (MM "Brain Injuries")                                                                            |  |
| S3 | TI ( ((head or brain) N3 (injur* or trauma)) ) OR AB ( ((head or brain) N3 (injur* or trauma)) ) |  |
| S4 | S1 OR S2 OR S3                                                                                   |  |
| S5 | (mild or moderate)                                                                               |  |
| S6 | (MH "Prospective Studies")                                                                       |  |

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| S7  | TI ( (cohort* or longitudinal or prospective or retrospective or follow-up or "follow up" or cross-section* or "cross section*" or "post-injur*" or "post injur*") ) OR AB ( (cohort* or longitudinal or prospective or retrospective or follow-up or "follow up" or cross-section* or "cross section*" or "post-injur*" or "post injur*") ) |  |
| S8  | S4 and S5 and (S6 or S7)                                                                                                                                                                                                                                                                                                                     |  |
| S9  | ("glasgow outcome scale" or gos)                                                                                                                                                                                                                                                                                                             |  |
| S10 | ("extended glasgow outcome scale" or gos-e or "gos e" or gose)                                                                                                                                                                                                                                                                               |  |
| S11 | ("rivermead post concussion symptoms questionnaire" or rpq)                                                                                                                                                                                                                                                                                  |  |
| S12 | ("euro qual" or "euro qual5d" or "euro qol5d" or eq-5d or "eq 5d" or eq5-d or eq5d or euroqual or euroqol or euroqual5d or euroqol5d)                                                                                                                                                                                                        |  |
| S13 | ("quality of life after brain injury" or qolibri)                                                                                                                                                                                                                                                                                            |  |
| S14 | (sf12 or "sf 12" or sf twelve or sftwelve)                                                                                                                                                                                                                                                                                                   |  |
| S15 | (sf36* or "sf 36*" or sf thirtysix or sf thirty six)                                                                                                                                                                                                                                                                                         |  |
| S16 | S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15                                                                                                                                                                                                                                                                                                 |  |
| S17 | (S8 AND S16)                                                                                                                                                                                                                                                                                                                                 |  |
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**Web of Science Science Citation Index Expanded (SCI-EXPANDED), Conference Proceedings Citation Index- Science (CPCI-S)**  
**21<sup>st</sup> May 2025**

| #  | Searches                                                                                                                                                                                                                                                                                                                                            |  |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| #1 | ((head or brain) NEAR/3 (injur* or trauma)) (Title) or ((head or brain) NEAR/3 (injur* or trauma)) (Abstract)                                                                                                                                                                                                                                       |  |
| #2 | (mild or moderate) (Title) or (mild or moderate) (Abstract)                                                                                                                                                                                                                                                                                         |  |
| #3 | ((cohort* or longitudinal or prospective or retrospective or follow-up or "follow up" or cross-section* or "cross section*" or "post-injur*" or "post injur*") (Title) or ((cohort* or longitudinal or prospective or retrospective or follow-up or "follow up" or cross-section* or "cross section*" or "post-injur*" or "post injur*") (Abstract) |  |
| #4 | ("glasgow outcome scale" or gos) (Title) or ("glasgow outcome scale" or gos) (Abstract)                                                                                                                                                                                                                                                             |  |
| #5 | ("extended glasgow outcome scale" or gos-e or "gos e" or gose) (Title) or ("extended glasgow outcome scale" or gos-e or "gos e" or gose) (Abstract)                                                                                                                                                                                                 |  |
| #6 | ("rivermead post concussion symptoms questionnaire" or rpq) (Title) or ("rivermead post concussion symptoms questionnaire" or rpq) (Abstract)                                                                                                                                                                                                       |  |
| #7 | ("euro qual" or "euro qual5d" or "euro qol5d" or eq-5d or "eq 5d" or eq5-d or eq5d or euroqual or euroqol or euroqual5d or euroqol5d) (Title) or ("euro qual" or "euro qual5d" or "euro qol5d" or eq-5d or "eq 5d" or eq5-d or eq5d or euroqual or euroqol or euroqual5d or euroqol5d) (Abstract)                                                   |  |

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| #8  | ("quality of life after brain injury" or qolibri) (Title) or ("quality of life after brain injury" or qolibri) (Abstract)                         |  |
| #9  | (sf12 or "sf 12" or sf-12 or sf twelve or sftwelve) (Title) or (sf12 or "sf 12" or sf-12 or sf twelve or sftwelve) (Abstract)                     |  |
| #10 | (sf36* or "sf 36*" or sf-36 or sf thirtysix or sf thirty six) (Title) or (sf36* or "sf 36*" or sf-36 or sf thirtysix or sf thirty six) (Abstract) |  |
| #11 | #1 and #2 and #3 and (#4 or #5 or #6 or #7 or #8 or #9 or #10)                                                                                    |  |
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For Peer Review Only/Not for Distribution

## Supplementary Material 2: Reasons for study exclusion

|                                                                                                                                                                                                                                                                                                                           | Reason Exclusion                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| 1) Abdulle AE, de Koning ME, van der Horn HJ, et al. Early Predictors for Long-Term Functional Outcome After Mild Traumatic Brain Injury in Frail Elderly Patients. <i>Journal of Head Trauma Rehabilitation</i> . 2018;33:E59-E67.                                                                                       | Outcomes not measured at required time points. |
| 2) Af Geijerstam JL, Oredsson S, Britton M. Medical outcome after immediate computed tomography or admission for observation in patients with mild head injury: Randomised controlled trial. <i>British Medical Journal</i> . 2006;333:465-468.                                                                           | Outcomes not measured at required time points  |
| 3) Agtarap S, Kramer MD, Campbell-Sills L, et al. Invariance of the Bifactor Structure of Mild Traumatic Brain Injury (mTBI) Symptoms on the Rivermead Postconcussion Symptoms Questionnaire Across Time, Demographic Characteristics, and Clinical Groups: A TRACK-TBI Study. <i>Assessment</i> . 2020:1073191120913941. | No relevant outcome reported.                  |
| 4) de Koning ME, Scheenen ME, van der Horn HJ, et al. Non-Hospitalized Patients with Mild Traumatic Brain Injury: The Forgotten Minority. <i>Journal of Neurotrauma</i> . 2017;34:257-261                                                                                                                                 | Outcomes not measured at required time points  |
| 5) Degos V, Lescot T, Icke C, et al. Computed tomography-estimated specific gravity at hospital admission predicts 6-month outcome in mild-to-moderate traumatic brain injury patients admitted to the intensive care unit. <i>Anesthesia &amp; Analgesia</i> . 2012;114:1026-1033.                                       | Outcomes not available                         |
| 6) Finnanger TG, Olsen A, Skandsen T, et al. Can depressive symptoms and global function in the first year after traumatic brain injury predict executive problems and emotional and behavioural symptoms 2-5 years post-injury? <i>Brain Injury</i> . 2014;28(5-6):629-630                                               | Wrong population                               |
| 7) Fure SC, Howe EI, Andelic N, et al. Cognitive and vocational rehabilitation after mild-to-moderate traumatic brain injury: a randomised controlled trial. <i>Annals of Physical &amp; Rehabilitation Medicine</i> . 2021:101538.                                                                                       | Outcomes not available                         |
| 8) de Kruijk JR, Leffers P, Meerhoff S, Rutten J, Twijnstra A. Effectiveness of bed rest after mild traumatic brain injury: a randomised trial of no versus six days of bed rest. <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> . 2002;73:167-172                                                            | Pre 2004                                       |
| 9) Gardner R, Ferguson A, Nielson J, et al. Functional outcome trajectories after traumatic brain injury: Novel insights from the cobrit study. <i>Journal of Neurotrauma</i> . 2017;34(13):A10                                                                                                                           | Wrong population                               |
| 10) Gardner RC, Cheng J, Ferguson AR, et al. Divergent 6-month functional outcome trajectories and predictors after traumatic brain injury. <i>Journal of Neurotrauma</i> . 2018;35(16):A156-A157.                                                                                                                        | Wrong population                               |
| 11) Gaudette E, Seabury SA, Goldman DP, Manley GT, Markowitz A. Return to work after mild traumatic brain injury-the protective effect of education: A track-TBI study. <i>Journal of Neurotrauma</i> . 2018;35(16):A147.                                                                                                 | Wrong population                               |
| 12) Hall EC, Lund E, Brown D, et al. How are you really feeling? A prospective evaluation of cognitive function following trauma. <i>The Journal of Trauma and Acute Care Surgery</i> . 2014;76:859-864; discussion 864-855.                                                                                              | Wrong population                               |
| 13) Heijenbrok-Kal M, Van Baalen B, Ribbers G. Long-term functional outcome following moderate to severe traumatic brain injury. <i>Brain Injury</i> . 2010;24(3):360-361.                                                                                                                                                | Wrong population                               |
| 14) Henninger N, Izzy S, Carandang R, Hall W, Muehlschlegel S. Severe leukoariosis portends a poor outcome after traumatic brain injury. <i>Neurocritical Care</i> . 2014;21:483-495.                                                                                                                                     | Outcomes reported for wrong population         |
| 15) Hou R, Moss-Morris R, Peveler R, et al. How does a trivial head injury result in enduring symptoms? A prospective investigation of outcome after mild traumatic brain injury. <i>European Neuropsychopharmacology</i> . 2011;21:S332-S333.                                                                            | Non-applicable outcomes                        |
| 16) Kleffeltgaard I, Roe C, Sandvik L, Hellstrom T, Soberg HL. Measurement properties of the high-level mobility assessment tool for mild traumatic brain injury. <i>Physical Therapy</i> . 2013;93:900-910.                                                                                                              | Non-applicable outcomes                        |
| 17) Levin HS, Boake C, Song J, et al. Validity and sensitivity to change of the extended Glasgow Outcome Scale in mild to moderate traumatic brain injury. <i>Journal of Neurotrauma</i> . 2001;18:575-584.                                                                                                               | Outcomes not measured at required time points  |
| 18) Liu S, Junn C, Hoffman J. The Role of Resilience on Headache After Mild Traumatic Brain Injury. <i>Archives of Physical Medicine and Rehabilitation</i> . 2019;100(10):e134.                                                                                                                                          | Outcomes not measured at required time points  |
| 19) Luoto TM, Iverson GL, Losoi H, Lehtimäki T, Ohman J. A prospective study of the ApoE gene as a predictor of mild traumatic brain injury outcome. <i>Brain Injury</i> . 2014;28(5-6):678.                                                                                                                              | Non-applicable outcomes                        |

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| 20) Mazlan M, Roslan NF. Post-concussion syndrome and quality-of-life after mild traumatic brain injury in Malaysian patients. <i>Brain Injury</i> . 2016;30 (5-6):680.                                                                                                                                                                        | Outcomes not measured at required time points |
| 21) McMahon PJ, Hricik AJ, Pardini J, Puccio A, Okonkwo DO. Post-concussion symptoms and functional outcome in mild traumatic brain injury: Results from the prospective track-TBI study. <i>Journal of Neurotrauma</i> . 2013;30 (15):A19-A20.                                                                                                | Duplication of reported study data            |
| 22) Miller KJ, Schwab KA, Warden DL. Predictive value of an early Glasgow Outcome Scale score: 15-month score changes. <i>Journal of Neurosurgery</i> . 2005;103:239-245.                                                                                                                                                                      | Outcomes not measured at required time points |
| 23) Nelson LD, Ranson J, Ferguson AR, et al. Validating Multi-Dimensional Outcome Assessment Using the Traumatic Brain Injury Common Data Elements: An Analysis of the TRACK-TBI Pilot Study Sample. <i>Journal of Neurotrauma</i> . 2017;34:3158-3172.                                                                                        | Wrong population                              |
| 24) Nishijima DK, Gaona SD, Faul M, et al. The Association of Trauma Center Transport and Long-term Functional Outcomes in Head-injured Older Adults Transported by Emergency Medical Services. <i>Academic Emergency Medicine</i> . 2020;27:207-216.                                                                                          | Wrong population                              |
| 25) Saksvik S, Karaliute M, Kallestad H, Karlsen R, Skandsen T, Olsen A. Sleep disturbances and fatigue predicts postconcussive symptoms 12 months after mild traumatic brain injury. <i>Brain Injury</i> . 2017;31 (6-7):926-927.                                                                                                             | Outcome not available                         |
| 26) Sandhaug M, Andelic N, Langhammer B, Mygland A. Functional level during the first 2 years after moderate and severe traumatic brain injury. <i>Brain Injury</i> . 2014;28 (5-6):597.                                                                                                                                                       | Duplicated study data                         |
| 27) Shepherd D, Heinonen-Guzejev M, Heikkila K, Landon J, Theadom A. Sensitivity to Noise Following a Mild Traumatic Brain Injury: A Longitudinal Study. <i>Journal of Head Trauma Rehabilitation</i> . 2021;22:22.                                                                                                                            | Outcomes not measured at required time points |
| 28) Sigurdardottir S, Andelic N, Roe C, Schanke AK. Cognitive recovery trajectories over the first five years following moderate-to-severe traumatic brain injury. <i>Brain Injury</i> . 2017;31 (6-7):854-855.                                                                                                                                | Wrong population                              |
| 29) Skandsen T, Finnanger TG, Andersson S, Lydersen S, Brunner JF, Vik A. Cognitive impairment 3 months after moderate and severe traumatic brain injury: a prospective follow-up study. <i>Archives of Physical Medicine &amp; Rehabilitation</i> . 2010;91:1904-1913.                                                                        | Wrong population                              |
| 30) Soberg HL, Andelic N, Langhammer B, Tamber AL, Bruusgaard KA, Kleffjellgaard I. Effect of vestibular rehabilitation on change in health-related quality of life in patients with dizziness and balance problems after traumatic brain injury: A randomized controlled trial. <i>Journal of Rehabilitation Medicine</i> . 2021;53:jrm00181. | Wrong population                              |
| 31) Sullivan K, Hall E, Galvagno S, et al. Mild traumatic brain injury is not 'mild' trauma survivors tell their complicated stories. <i>Anesthesia and Analgesia</i> . 2018;126 (4 Supplement 1):777-779.                                                                                                                                     | Outcomes not measured at required time points |
| 32) Sveen U, Bautz-Holter E, Sandvik L, Alvsaker K, Roe C. Relationship between competency in activities, injury severity, and post-concussion symptoms after traumatic brain injury. <i>Scandinavian Journal of Occupational Therapy</i> . 2010;17:225-232.                                                                                   | Outcomes not measured at required time points |
| 33) Temkin NR, Zahniser E, Morrissey MR, et al. I. Glasgow outcome scale extended-disability from only tbi vs all injuries in those with gcs 13-15: A track-TBI study. <i>Journal of Neurotrauma</i> . 2018;35 (16):A67-A68.                                                                                                                   | Outcomes not measured at required time points |
| 34) Temkin N, Sattris G, Machamer J, Morrissey MR, Manley G, Dikmen S. Glasgow outcome scale extended-differences counting disability from only brain injury versus brain and other system injuries. <i>Journal of Neurotrauma</i> . 2017;34 (13):A86.                                                                                         | Wrong population                              |
| 35) Thastum MM, Rask CU, Naess-Schmidt ET, et al. Design of an early intervention for persistent post-concussion symptoms in adolescents and young adults: A feasibility study. <i>Neurorehabilitation</i> . 2018;43:155-167.                                                                                                                  | Outcomes not measured at required time points |
| 36) Theadom A, Barker-Collo S, Jones KM, Parmar P, Bhattacharjee R, Feigin VL. MLC901 (NeuroAiD II TM) for cognition after traumatic brain injury: a pilot randomized clinical trial. <i>European Journal of Neurology</i> . 2018;25:1055-e1082.                                                                                               | Outcomes not measured at required time points |
| 37) Thomas M, Skilbeck C, Cannan P, Slatyer M. The Structure of the Rivermead Post-Concussion Symptoms Questionnaire in Australian Adults with Traumatic Brain Injury. <i>Brain Impairment</i> . 2018;19:166-182.                                                                                                                              | Wrong population                              |
| 38) Thompson H, Rivara F, Temkin N, Becker K, Maier R. Relationship of metabolomic profile and functional trajectory following mild traumatic brain injury in older adults. <i>Journal of Neurotrauma</i> . 2019;36 (13):A29.                                                                                                                  | Outcomes not measured at required time points |
| 39) Thompson H, Rue T, Rivara F. Natural history of symptoms and symptom severity following geriatric traumatic brain injury. <i>Journal of Neurotrauma</i> . 2012;29 (10):A189-A190.                                                                                                                                                          | Outcomes not measured at required time points |
| 40) Tolli A, Hoybye C, Bellander BM, Borg J. Clinical course and outcome of cognitive impairments after traumatic brain injury or aneurysmal subarachnoid haemorrhage. <i>Neurorehabilitation and Neural Repair</i> . 2018;32 (4-5):466.                                                                                                       | Wrong population                              |

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| 41) van der Horn HJ, Vergara VM, Espinoza FA, Calhoun VD, Mayer AR, van der Naalt J. Functional outcome is tied to dynamic brain states after mild to moderate traumatic brain injury. <i>Human Brain Mapping</i> . 2020;41:617-631.                                                                                                                                                                                                                                  | Outcomes not measured at required time points |
| 42) Voormolen DC, Polinder S, von Steinbuechel N, Vos PE, Cnossen MC, Haagsma JA. The association between post-concussion symptoms and health-related quality of life in patients with mild traumatic brain injury. <i>Injury</i> . 2019;50:1068-1074.                                                                                                                                                                                                                | Outcomes not measured at required time points |
| 43) Willemse-van Son AH, Ribbers GM, Hop WC, van Duijn CM, Stam HJ. Association between apolipoprotein-epsilon4 and long-term outcome after traumatic brain injury. <i>Journal of Neurology, Neurosurgery &amp; Psychiatry</i> . 2008;79:426-430.                                                                                                                                                                                                                     | Wrong population                              |
| 44) Yue JK, Satris GG, Dalle Ore CL, et al. Polytrauma Is Associated with Increased Three- and Six-Month Disability after Traumatic Brain Injury: A TRACK-TBI Pilot Study. <i>Neurotrauma Reports</i> . 2020;1:32-41.                                                                                                                                                                                                                                                 | Wrong population                              |
| 45) Campbell-Sills L, Jain S, Sun X, et al. Risk Factors for Suicidal Ideation Following Mild Traumatic Brain Injury: A TRACK-TBI Study. <i>Journal of Head Trauma Rehabilitation</i> . 2021;36:E30-E39.                                                                                                                                                                                                                                                              | Non-applicable outcomes                       |
| 46) Rauen K, Reichelt L, Probst P, et al. Quality of life up to 10 years after traumatic brain injury: a cross-sectional analysis. <i>Health &amp; Quality of Life Outcomes</i> . 2020;18:166.                                                                                                                                                                                                                                                                        | Outcomes not measured at required time points |
| 47) Singh R, Choudhri K, Sinha S, Mason S, Lecky F, Dawson J. Global outcome after traumatic brain injury in a prospective cohort. <i>Clinical Neurology &amp; Neurosurgery</i> . 2019;186:105526                                                                                                                                                                                                                                                                     | Outcomes not measured at required time points |
| 48) Booker J. Predicting recovery after mild TBI. <i>Neurosurgery</i> . 2019;84 (5):E274.                                                                                                                                                                                                                                                                                                                                                                             | Outcomes not measured at required time points |
| 49) Yue JK, Levin HS, Suen CG, et al. Age and sex-mediated differences in six-month outcomes after mild traumatic brain injury in young adults: a TRACK-TBI study. <i>Neurological Research</i> . 2019;41:609-623.                                                                                                                                                                                                                                                    | Outcomes not measured at required time points |
| 50) Einarsen CE, van der Naalt J, Jacobs B, et al. Moderate Traumatic Brain Injury: Clinical Characteristics and a Prognostic Model of 12-Month Outcome. <i>World Neurosurgery</i> . 2018;114:e1199-e1210.                                                                                                                                                                                                                                                            | Outcomes not measured at required time points |
| 51) De Koning M, Scheenen M, Van Der Horn H, Spikman J, Van Der Naalt J. From miserable minority to the fortunate few: The other end of the mild traumatic brain injury spectrum. <i>Brain Injury</i> . 2017;31 (6-7):798.                                                                                                                                                                                                                                            | Outcomes not measured at required time points |
| 52) Grauwmeijer E, Heijenbrok-Kal MH, Peppel LD, et al. Cognition, Health-Related Quality of Life, and Depression Ten Years after Moderate to Severe Traumatic Brain Injury: A Prospective Cohort Study. <i>Journal of Neurotrauma</i> . 2018;35:1543-1551.                                                                                                                                                                                                           | Wrong population                              |
| 53) Yue JK, Winkler EA, Sharma S, et al. Temporal profile of care following mild traumatic brain injury: predictors of hospital admission, follow-up referral and six-month outcome. <i>Brain Injury</i> . 2017;31:1820-1829.                                                                                                                                                                                                                                         | Outcomes not measured at required time points |
| 54) van der Naalt J, Timmerman ME, de Koning ME, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. <i>Lancet Neurology</i> . 2017;16:532-540.                                                                                                                                                                                                                                                            | Outcomes not measured at required time points |
| 55) Dikmen S, Machamer J, Temkin N. Mild Traumatic Brain Injury: Longitudinal Study of Cognition, Functional Status, and Post-Traumatic Symptoms. <i>Journal of Neurotrauma</i> . 2017;34:1524-1530.                                                                                                                                                                                                                                                                  | Outcomes not measured at required time points |
| 56) de Koning ME, Scheenen ME, van der Horn HJ, et al. Outpatient follow-up after mild traumatic brain injury: Results of the UPFRONT-study. <i>Brain Injury</i> . 2017;31:1102-1108.                                                                                                                                                                                                                                                                                 | Outcomes not measured at required time points |
| 57) Beal ML, Psoter KJ, Bechtold KT, et al. Relationship Between Posttraumatic Headache and Depression After Mild Traumatic Brain Injury. <i>J Neuropsychiatry Clin Neurosci</i> . 2024;appineuropsych20230143.                                                                                                                                                                                                                                                       | Non-applicable outcomes                       |
| 58) Diaz M, Gardner R, Manley G, Puccio A, Okonkwo D, Giacino J, Bodien Y. Transforming research & clinical knowledge in geriatric traumatic brain injury (trackgeri) pilot study: Role of proxy informants. <i>J Neurotrauma</i> . 2021;38(14):A19.                                                                                                                                                                                                                  | Non-applicable outcomes                       |
| 59) Howe E, Andelic N, Fure SC, Lovstad M, Roe C, Aas E. Effect of a Combined Cognitive and Vocational Intervention on Change in HRQoL after TBI. <i>Archives of Physical Medicine and Rehabilitation</i> . 2022;103(12):e100.                                                                                                                                                                                                                                        | Outcomes not measured at required time points |
| 60) Howe EI, Andelic N, Fure SCR, et al. Cost-effectiveness analysis of combined cognitive and vocational rehabilitation in patients with mild-to-moderate TBI: results from a randomized controlled trial. <i>BMC Health Serv Res</i> . 2022;22:185.                                                                                                                                                                                                                 | Non-applicable outcomes                       |
| 61) Machamer J, Temkin N, Dikmen S, et al. Symptom Frequency and Persistence in the First Year after Traumatic Brain Injury: A TRACK-TBI Study. <i>J Neurotrauma</i> . 2022;39:358-370.                                                                                                                                                                                                                                                                               | Duplicate                                     |
| 62) Monti, Daniel A. MD; Faezeh, Vedaiei MS; Zabrecky, George DC, MD; Alizadeh, Mahdi PhD; Wintering, Nancy MSW; Bazzan, Anthony J. MD; Mohamed, Feroze B. PhD; Newberg, Andrew B. MD. Changes in Resting-State Functional Connectivity and Cognitive-Affective Symptoms in Patients With Post-Concussion Syndrome Treated With N-Acetyl Cysteine. <i>Journal of Head Trauma Rehabilitation</i> 40(3):p E196-E207, May/June 2025.   DOI: 10.1097/HTR.0000000000000976 | Outcomes not measured at required time points |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                              |
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| 63) Shawn R. Eagle, <sup>1</sup> Nancy Temkin, <sup>2</sup> Jason K. Barber, <sup>2</sup> Michael McCrea, <sup>3</sup> Joseph T. Giacino, <sup>4</sup> David Okonkwo, <sup>1</sup> Geoffrey T. Manley, <sup>5</sup> and Lindsay Nelson, <sup>3</sup> for the TRACK-TBI Investigators Association of Subacute Mild Traumatic Brain Injury Symptoms With Long-Term Persistent Symptoms, Functional Limitations, and Quality of Life <i>Neurology</i> ® 2025;104:e213427. doi:10.1212/WNL.000000000000213427                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Does not report outcome trajectory for 3 and 6 months        |
| 64. Prof. Pavel I. Pilipenko, MD, PhD; <sup>1</sup> Dr Anna A. Ivanova, MD; <sup>2</sup> Dr Yulia V. Kotsiubinskaya, MD, PhD; <sup>3</sup> 5 Prof. Vera N. Grigoryeva, MD, PhD; <sup>4</sup> A/Prof. Alexey Y. Khrulev, MD, PhD; <sup>4</sup> Dr Anatoly V. Skorokhodov, 6 MD; <sup>5</sup> Dr Maxim M. Gavrik, MD; <sup>6</sup> Dr. Nona N. Mkrtchan, MD; <sup>7</sup> Prof. Marek Majdan, PhD; <sup>8</sup> Prof. Peter 7 Valkovic, MD, PhD; <sup>9</sup> Dr Daria Babarova, PhD; <sup>8</sup> Prof. Suzanne Barker-Collo, PhD; <sup>10</sup> A/Prof. Kelly Jones, 8 PhD; <sup>11</sup> Prof. Valery L. Feigin, MD, PhD A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED, MULTI-CENTRE, PHASE III STUDY OF 2 MLC901 (NEUROAID IITM) FOR THE TREATMENT OF COGNITIVE IMPAIRMENT AFTER MILD 3 TRAUMATIC BRAIN INJURY medRxiv 2024.08.28.24312757; doi: <a href="https://doi.org/10.1101/2024.08.28.24312757">https://doi.org/10.1101/2024.08.28.24312757</a> | Does not report outcomes at required time points post injury |

Supplementary Material 3: Summary of included studies

| Refere<br>nce  | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Study Design                                                                                                                                                                           |  | Outcomes                                                  | Time<br>points<br>and<br>factors                                          | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
| 1 <sup>1</sup> | <p>Inclusion Criteria</p> <ul style="list-style-type: none"><li>• Moderate TBI (Glasgow Coma Scale or GCS of 9 to 13)</li><li>• Age 18 to 60 years old</li><li>• Closed head injury occurred within two days of MLC601 administration</li><li>• TBI with conservative/nonsurgical management</li><li>• Medically stable with no major systemic comorbidities or metabolic abnormalities</li></ul> <p>2.2. Exclusion Criteria</p> <ul style="list-style-type: none"><li>• Intracranial lesion on initial imaging or during observation for which surgery is indicated</li><li>• Bilateral unreactive pupil</li><li>• Spinal cord injury</li><li>• History of cardiopulmonary arrest during treatment</li><li>• Life-threatening status</li></ul> | <p>Single centre pilot RCT of MLC601 (traditional Chinese medicine) neither double blind or placebo controlled.</p> <p>Medication + usual care versus usual care.</p> <p>Indonesia</p> |  | <p>Glasgow Outcome Scale (GOS) and Barthel Index (BI)</p> | <p>Discharge and at months (M) 3 and 6</p> <p>Factor assessed: MLC601</p> | <p>16 control group</p> <p>16 intervention group</p> <p>Control v Intervention Median GOS (IQR)(Range)</p> <p><b>Discharge</b></p> <p>2.5 (IQR 0.5) (Min max 2–3) v 3.0 (IQR 0.375) (Min max 2-3)</p> <p><b>Month 3</b></p> <p>3.0 (IQR 0.0) (Min max 2–4) v 3.0 (IQR0.5) (Min max 2–4)</p> <p><b>Month 6</b></p> <p>3.5 (IQR 0.5) (Min max 2–4) v 3.5 (IQR 0.5) (Min max 2–4)</p> <p>Control v Intervention BI (IQR) (Range)</p> <p><b>Discharge</b></p> <p>22.5 (IQR 7.5) (Min max 10–55) v 40.0 (IQR 16.25) (Min Max 10-55)</p> <p><b>Month 3</b></p> <p>35.0 (IQR 11.875) (Min max 15–65) v 47.5 (IQR 11.875) (Min max 25–75)</p> <p><b>Month 6</b></p> <p>57.5 (IQR 14.375) (Min Max 25–75) v 67.5 (IQR 15.0) (Min max30–80)</p> | Not specified                                                                | Not specified                                                           | 15                   |

| Refere<br>nce  | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Study Design                                                                                               |  | Outcomes                                                                                                                                                      | Time<br>points<br>and<br>factors            | Results                                                                                                                                                                                                                                                                       | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up                               | Quality<br>appraisal |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|----------------------|
| 2 <sup>2</sup> | <p>mTBI patient with matched healthy controls</p> <p>Inclusion criteria:</p> <p>GCS 13–15 at hospital admission, normal posttraumatic CT findings,</p> <p>and one or more:</p> <p>LOC ( up to 30 minutes)</p> <p>presence of altered mental state at the time of the incident,</p> <p>post-traumatic amnesia (&lt; 60 min), and/or retrograde amnesia (&lt; 30 min).</p> <p>patients had to have reported clinical impairments within 1 week after the injury</p> <p>Exclusion criteria:</p> <p>Age&lt;17or&gt;64</p> <p>History of neurologic or psychiatric disease, neurosurgical intervention or TBI; current and past drug or alcohol abuse; concussion&lt;3 months before index injury</p> | <p>Longitudinal cohort study with recruitment at emergency units of</p> <p>4 hospitals in Switzerland.</p> |  | <p>Rivermead Post Concussion Symptoms</p> <p>Questionnaire (RPQ 13 items excluding headache, dizziness and nausea)</p> <p>Beck Depression Inventory (BDI)</p> | <p>1 week</p> <p>3 months</p> <p>1 year</p> | <p>35 mTBI patients 35 controls</p> <p><b>1 week mean (SD)</b></p> <p>mTBI: 15.51 (8.04) control 2.23 (3.58)</p> <p><b>3 months mean (SD)</b></p> <p>mTBI: 8.97 (10.57) control: 1.63 (4.22)</p> <p><b>1 year mean (SD)</b></p> <p>mTBI: 6.69 (9.52) control: 2.14 (4.28)</p> | 100% of 35                                                                   | <p>100% at 12 months no loss to follow up</p> <p>3 with most severe RPQ did not improve over time</p> | 13                   |

| Reference      | Population                                                                                                                                                                                                                                                                                                                                                                                                              | Study Design                                                                                                                                                                      |  | Outcomes                                                                                                                                                                                     | Time points and factors                                                                                                                                                 | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | % (n) of acute injury population enrolled with 3 month follow up                | % of 3 month population with six and/or twelve month follow up | Quality appraisal |
|----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|----------------------------------------------------------------|-------------------|
| 3 <sup>3</sup> | <p>Glasgow Coma Scale (GCS) score 13–15 on arrival to the Inclusion criteria: Emergency Department (ED) and eligibility for Computed Tomography (CT) head due to head trauma according to NICE guidelines.</p> <p>Patients with a history of previous TBI, psychiatric or neurological disorder were excluded. Participants were included in this analysis only if they attended a minimum of one follow-up session</p> | <p>Prospective longitudinal study comparing mTBI patients to healthy and extra-cranially injured controls.</p> <p>Recruitment at single Major Trauma Center (MTC) in England.</p> |  | <p>Glasgow Outcome Scale Extended (GOSE)</p> <p>Rivermead Post-Concussion Symptoms Questionnaire (RPQ)</p> <p>Quality of Life after Brain Injury (QOLIBRI) assessed; health-related QoL;</p> | <p>Face-to-face assessment of health, quality of life (QoL) and cognitive function were completed at: 2 weeks, 3 months, 6 months, 1 year and 2 years after injury.</p> | <p>N=61 For mTBI group:</p> <p>Mean GOSE <b>3 months</b>      <b>6 month</b>      <b>1 year</b>    <b>2 years</b></p> <p>7.3                      7.5                      7.4            7.4</p> <p>Mean RPQ (% with &gt;2 new post concussive symptoms)</p> <p><b>2 week</b>    <b>3 months</b>      <b>6 month</b>      <b>1 year</b>      <b>2 yr</b></p> <p>14 (32%)    10.8 (28%)    10.8 (23%)    10.8 (18%)    10.9 (22%)</p> <p>Mean Quality of Life after Brain Injury (QOLIBRI)</p> <p><b>2 week</b>      <b>3 months</b>      <b>6 month mean</b> <b>1 year mean</b> <b>2 years</b></p> <p>75              80              80              81              82</p> | 85% of 61                                                                       | <p>6 months 79%</p> <p>12 months 65%</p>                       | 12                |
| 4 <sup>4</sup> | <p>Initial GCS 13 or more were aged 18 or more and provided an informed consent to participate and to be called by phone after their discharge.</p>                                                                                                                                                                                                                                                                     | <p>2 centre prospective cohort study.</p>                                                                                                                                         |  | <p>Rivermead Post-Concussion Symptoms Questionnaire (RPQ)</p> <p>Rivermead Head</p>                                                                                                          | <p>130 patients initially recruited from 1154 approached</p>                                                                                                            | <p>➤ 3 new RPQ post-concussive symptoms, n (%)</p> <p>Baseline interview, 71 (54.6%)</p> <p><b>15 days</b> post-injury interview, 56 (47.4%)</p> <p><b>1 month</b> post-injury interview, 42 (40%)</p> <p><b>3 months</b> post-injury interview, 20 (22%)</p> <p><b>6 months</b> post-injury interview, 12 (21.4%)</p>                                                                                                                                                                                                                                                                                                                                                        | <p>8% of 1154 approached were enrolled</p> <p>75% of 130 initially enrolled</p> | <p>62% (56) at 6 months</p>                                    | 12                |

| Refere<br>nce  | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Study Design                                                                                                                                                                                                                         |  | Outcomes                                                                                                                                                                                                                                 | Time<br>points<br>and<br>factors                                | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
|                | Patient recruited from emergency department of Sfax or Deguach in Tunisia between September 1, 2013 and March 31, 2014. 5 negative ED CT scans rest no CT evaluation                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                      |  | Injury Follow-up Questionnaire (RHFUQ)                                                                                                                                                                                                   | 91 at 3 months<br><br>By 6 months only 56 not lost to follow-up | Any impact according to RHFUQ, n (%)<br><br><b>1 month</b> post-injury interview, 39 (37.1%)<br><br><b>3 months</b> post-injury interview, 18 (19.8%)<br><br><b>6 months</b> post-injury interview, 9 (16.1%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                              |                                                                         |                      |
| 5 <sup>5</sup> | Inclusion criteria: were evidence of trauma preceding a brain injury and at least 1 of: (a) LOC (b) post-traumatic amnesia less than 24 h (if present), and (c) a Glasgow Coma Scale (GCS) score between 13 and 15 after 30 min following the injury.<br><br>Exclusion criteria were:<br><br>(a) age under 20; (b) previous symptomatic brain injury; (c) history of a psychiatric disorder; and (d) history of major substance abuse or another medical condition (frequently) associated with cognitive changes | Prospective longitudinal cohort study between March 2013 and May 2014 recruited from neurosurgical outpatient department (NSOPD) in Chiayi County District Hospitals in middle Taiwan<br><br>36 had intracranial injuries on CT scan |  | 1, 3, and 12 months after mTBI:<br><br>the Quality of Life after Brain Injury (QOLIBRI), Chinese version, 16-item<br><br>the Glasgow Outcome Scale Extended (GOSE),<br><br>Short Form 36 Health Survey (SF-36)<br><br>Post Concussion 16 | 100 participants<br><br>1, 3, and 12 months                     | Mean QOLIBRI score across 6 domains<br><br>41 patients "poor QoL baseline and recovering"<br><br><b>1 month</b> 2.3 <b>3 months</b> 2.5 <b>12 months</b> 3.5<br><br>Fine QoL baseline and recovering (n=59)<br><br><b>1 month</b> 3.5 <b>3 months</b> 3.5 <b>12 months</b> 3.7<br><br>Mean GOSE<br><br>Moderate recovery after TBI (n=18)<br><br><b>1 month</b> 6.8 <b>3 months</b> 7.0 <b>12 months</b> 7.7<br><br>Fine recovery after TBI (n=82)<br><br><b>1 Month</b> 7.6 <b>3 months</b> 8.0 <b>12 months</b> 8.0<br><br>Mean MCS SF-36<br><br>Persistently under average QOL (n=11)<br><br><b>1 month</b> 33 <b>3 months</b> 32 <b>12 months</b> 31<br><br>Persistently fine QOL (n=89)<br><br><b>1 month</b> 52 <b>3 months</b> 52 <b>12 months</b> 52 | 95% of 105                                                                   | Not specified                                                           | 12                   |

| Refere<br>nce  | Population                                                                                                                                                | Study Design                                                  |  | Outcomes                                                                                            | Time<br>points<br>and<br>factors                                 | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|--|-----------------------------------------------------------------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
|                |                                                                                                                                                           |                                                               |  | Symptom<br>Checklist<br>(PCS)                                                                       |                                                                  | Mean PCS SF-36<br><br>Under average QoL and worsening (n=14)<br><br><b>1 month</b> 40 <b>3 months</b> 39 <b>12 months</b> 32<br><br>Under average QoL and improving (n=35)<br><br><b>1 month</b> 40 <b>3 months</b> 42 <b>12 months</b> 49<br><br>Fine QoL and slight worsening (n=51)<br><br><b>1 month</b> 59 <b>3 months</b> 59 <b>12 months</b> 58<br><br>Mean number of PCS symptoms (Y/N response)<br>Moderate symptoms after TBI (n=54)<br><br><b>1 month</b> 4 <b>3 months</b> 3 <b>12 months</b> 2<br><br>Severe symptoms after TBI (n=46)<br><br><b>1 month</b> 10 <b>3 months</b> 9 <b>12 months</b> 6 |                                                                              |                                                                         |                      |
| 6 <sup>6</sup> | Christchurch Hospital<br><br>Closed head injury<br>patients GCS, score of<br>between 13 and 15 on<br>first assessment, without<br>falling below 13 at any | Single centre<br>prospective<br>longitudinal<br>cohort study. |  | SF-36<br>Health<br>Survey<br>(version 2)<br>(SF-36, 8<br>functional<br>scales and<br>two<br>summary | Patient<br>s<br>assesse<br>d<br>within<br>1 week<br>of<br>injury | 37 mild CHI patients.<br><br>Mean RPSQ score<br><br><b>1 week</b> 20 <b>3 months</b> 10 <b>6 months</b> 10 <b>12 months</b> 10<br><br>Mean RHIFQ score                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 100%                                                                         | 84%                                                                     | 10                   |

| Reference                                                                                                                  | Population                                                                                                                                                                                     | Study Design                                                                        |               | Outcomes                                                                                                                  | Time points and factors                                                            | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | % (n) of acute injury population enrolled with 3 month follow up                                                           | % of 3 month population with six and/or twelve month follow up | Quality appraisal |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                         |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |            |           |           |           |           |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                       |  |                         |               |               |              |               |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |   |   |   |   |   |   |  |  |  |
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------|---------------|--------------|-------------|------------|---------------|---------------|-----|--|--|----------------------------|------|------|------|------|------|------|---|--|--|----------------------------------------|----|----|----|---|---|---|---|-------------------------------------|--|-------------------------|-----------|-----------|-----------|-----------|-------------|-----------|---|--|--|----------------------------|------|------|------|------|------|------|---|--|--|----------------------------------------|---|---|---|---|---|---|---|---------------------------------------------------------------------------------------|--|-------------------------|---------------|---------------|---------------|--------------|---------------|---------------|---|--|--|----------------------------|------|------|------|------|------|------|---|--|--|----------------------------------------|----|----|----|----|----|----|---|-----------------------------|--|-------------------------|------------|-----------|-----------|-----------|-----------|-----------|---|--|--|----------------------------|------|------|------|------|------|------|---|--|--|----------------------------------------|---|---|---|---|---|---|---|-------------------------------------------------------|--|-------------------------|---------------|---------------|--------------|---------------|---------------|---------------|---|--|--|----------------------------|------|------|------|------|------|------|---|--|--|----------------------------------------|----|---|---|---|---|---|---|--|--|--|
|                                                                                                                            | consecutive assessment at the hospital.<br><br>Inclusion criteria: Age 15-56 years with negative CT, PTA< 24 hours and, no prior neurological conditions/tbi or intoxication at time of injury |                                                                                     |               | scores), the Rivermead Postconcussion Symptoms Questionnaire (RPSQ) Rivermead Head Injury Follow-up Questionnaire (RHIFQ) | (mean 5.5 ± 3.0 days) and then at 3 months (90 ± 5.5 days), 6 months and 12 months | <p>1 week 12 3 months 3 6 months 4</p> <p>SF-36 Physical (mean)</p> <p>1 week 44 3 months 56 6 months 56 12 months 56</p> <p>SF-36 Mental (mean)</p> <p>1 week 44 3 months 49 6 months 51 12 months 52</p> <table><tr><td colspan="10">Stepwise-forward multiple regression: associations between functional status at 1 week and health status at 3 and 6 months</td></tr><tr><td colspan="2">Independent measure pool</td><td colspan="8">Health assessment measures at 3 and 6 months post-injury (dependent variable)</td></tr><tr><td colspan="2"></td><td colspan="2">SF-36 Physical summary</td><td colspan="2">SF-36 Mental summary</td><td colspan="2">PCS sum (RPSQ total)</td><td colspan="2"></td></tr><tr><td colspan="2"></td><td>3 months</td><td>6 months</td><td>3 months</td><td>6 months</td><td>3 months</td><td>6 months</td><td colspan="2"></td></tr><tr><td colspan="2"></td><td>p-level</td><td>p-level</td><td>p-level</td><td>p-level</td><td>p-level</td><td>p-level</td><td colspan="2"></td></tr><tr><td colspan="2">Saccades only</td><td>Adjusted R<sup>2</sup></td><td>0.78 &lt;0.00001</td><td>0.70 0.00003</td><td>0.74 0.0002</td><td>0.43 0.002</td><td>0.70 &lt;0.00001</td><td>0.65 &lt;0.00001</td><td>0.6</td></tr><tr><td colspan="2"></td><td>Standard error of estimate</td><td>2.06</td><td>2.97</td><td>3.20</td><td>5.51</td><td>5.44</td><td>6.45</td><td>4</td></tr><tr><td colspan="2"></td><td>Number of qualifying measures in model</td><td>14</td><td>10</td><td>16</td><td>7</td><td>8</td><td>6</td><td>6</td></tr><tr><td colspan="2">Upper-limb visuomotor measures only</td><td>Adjusted R<sup>2</sup></td><td>0.20 0.02</td><td>0.22 0.02</td><td>0.08 0.05</td><td>0.13 0.13</td><td>0.49 0.0003</td><td>0.20 0.03</td><td>0</td></tr><tr><td colspan="2"></td><td>Standard error of estimate</td><td>4.35</td><td>4.48</td><td>7.42</td><td>6.66</td><td>7.09</td><td>9.50</td><td>2</td></tr><tr><td colspan="2"></td><td>Number of qualifying measures in model</td><td>3</td><td>4</td><td>1</td><td>7</td><td>7</td><td>5</td><td>4</td></tr><tr><td colspan="2">Combined eye and arm motor measures (saccades, oculomotor smooth pursuit, upper-limb)</td><td>Adjusted R<sup>2</sup></td><td>0.85 &lt;0.00001</td><td>0.85 &lt;0.00001</td><td>0.89 &lt;0.00001</td><td>0.73 0.00005</td><td>0.86 &lt;0.00001</td><td>0.81 &lt;0.00001</td><td>0</td></tr><tr><td colspan="2"></td><td>Standard error of estimate</td><td>1.72</td><td>2.06</td><td>2.17</td><td>3.83</td><td>3.83</td><td>4.80</td><td>1</td></tr><tr><td colspan="2"></td><td>Number of qualifying measures in model</td><td>12</td><td>15</td><td>12</td><td>13</td><td>10</td><td>13</td><td>4</td></tr><tr><td colspan="2">Neuropsychological measures</td><td>Adjusted R<sup>2</sup></td><td>0.32 0.003</td><td>0.28 0.01</td><td>0.13 0.08</td><td>0.24 0.02</td><td>0.22 0.02</td><td>0.17 0.03</td><td>0</td></tr><tr><td colspan="2"></td><td>Standard error of estimate</td><td>4.07</td><td>4.38</td><td>7.32</td><td>6.31</td><td>8.73</td><td>9.55</td><td>3</td></tr><tr><td colspan="2"></td><td>Number of qualifying measures in model</td><td>4</td><td>6</td><td>4</td><td>5</td><td>4</td><td>3</td><td>2</td></tr><tr><td colspan="2">Health status measures (all items SF-36, RPSQ, RHIFQ)</td><td>Adjusted R<sup>2</sup></td><td>0.79 &lt;0.00001</td><td>0.70 &lt;0.00001</td><td>0.54 0.00001</td><td>0.69 &lt;0.00001</td><td>0.70 &lt;0.00001</td><td>0.68 &lt;0.00001</td><td>0</td></tr><tr><td colspan="2"></td><td>Standard error of estimate</td><td>2.25</td><td>2.78</td><td>5.24</td><td>3.95</td><td>5.42</td><td>6.00</td><td>2</td></tr><tr><td colspan="2"></td><td>Number of qualifying measures in model</td><td>16</td><td>8</td><td>4</td><td>9</td><td>8</td><td>8</td><td>3</td></tr></table> | Stepwise-forward multiple regression: associations between functional status at 1 week and health status at 3 and 6 months |                                                                |                   |  |  |  |  |  |  |  | Independent measure pool |  | Health assessment measures at 3 and 6 months post-injury (dependent variable) |  |  |  |  |  |  |  |  |  | SF-36 Physical summary |  | SF-36 Mental summary |  | PCS sum (RPSQ total) |  |  |  |  |  | 3 months | 6 months | 3 months | 6 months | 3 months | 6 months |  |  |  |  | p-level | p-level | p-level | p-level | p-level | p-level |  |  | Saccades only |  | Adjusted R <sup>2</sup> | 0.78 <0.00001 | 0.70 0.00003 | 0.74 0.0002 | 0.43 0.002 | 0.70 <0.00001 | 0.65 <0.00001 | 0.6 |  |  | Standard error of estimate | 2.06 | 2.97 | 3.20 | 5.51 | 5.44 | 6.45 | 4 |  |  | Number of qualifying measures in model | 14 | 10 | 16 | 7 | 8 | 6 | 6 | Upper-limb visuomotor measures only |  | Adjusted R <sup>2</sup> | 0.20 0.02 | 0.22 0.02 | 0.08 0.05 | 0.13 0.13 | 0.49 0.0003 | 0.20 0.03 | 0 |  |  | Standard error of estimate | 4.35 | 4.48 | 7.42 | 6.66 | 7.09 | 9.50 | 2 |  |  | Number of qualifying measures in model | 3 | 4 | 1 | 7 | 7 | 5 | 4 | Combined eye and arm motor measures (saccades, oculomotor smooth pursuit, upper-limb) |  | Adjusted R <sup>2</sup> | 0.85 <0.00001 | 0.85 <0.00001 | 0.89 <0.00001 | 0.73 0.00005 | 0.86 <0.00001 | 0.81 <0.00001 | 0 |  |  | Standard error of estimate | 1.72 | 2.06 | 2.17 | 3.83 | 3.83 | 4.80 | 1 |  |  | Number of qualifying measures in model | 12 | 15 | 12 | 13 | 10 | 13 | 4 | Neuropsychological measures |  | Adjusted R <sup>2</sup> | 0.32 0.003 | 0.28 0.01 | 0.13 0.08 | 0.24 0.02 | 0.22 0.02 | 0.17 0.03 | 0 |  |  | Standard error of estimate | 4.07 | 4.38 | 7.32 | 6.31 | 8.73 | 9.55 | 3 |  |  | Number of qualifying measures in model | 4 | 6 | 4 | 5 | 4 | 3 | 2 | Health status measures (all items SF-36, RPSQ, RHIFQ) |  | Adjusted R <sup>2</sup> | 0.79 <0.00001 | 0.70 <0.00001 | 0.54 0.00001 | 0.69 <0.00001 | 0.70 <0.00001 | 0.68 <0.00001 | 0 |  |  | Standard error of estimate | 2.25 | 2.78 | 5.24 | 3.95 | 5.42 | 6.00 | 2 |  |  | Number of qualifying measures in model | 16 | 8 | 4 | 9 | 8 | 8 | 3 |  |  |  |
| Stepwise-forward multiple regression: associations between functional status at 1 week and health status at 3 and 6 months |                                                                                                                                                                                                |                                                                                     |               |                                                                                                                           |                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                   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| Independent measure pool                                                                                                   |                                                                                                                                                                                                | Health assessment measures at 3 and 6 months post-injury (dependent variable)       |               |                                                                                                                           |                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                   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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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|                                                                                                                            |                                                                                                                                                                                                | SF-36 Physical summary                                                              |               | SF-36 Mental summary                                                                                                      |                                                                                    | PCS sum (RPSQ total)                                                                                                                                                                                                                                                                                                                                                              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|                                                                                                                            |                                                                                                                                                                                                | 3 months                                                                            | 6 months      | 3 months                                                                                                                  | 6 months                                                                           | 3 months                                                                                                                                                                                                                                                                                                                                                                          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|                                                                                                                            |                                                                                                                                                                                                | p-level                                                                             | p-level       | p-level                                                                                                                   | p-level                                                                            | p-level                                                                                                                                                                                                                                                                                                                                                                           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| Saccades only                                                                                                              |                                                                                                                                                                                                | Adjusted R <sup>2</sup>                                                             | 0.78 <0.00001 | 0.70 0.00003                                                                                                              | 0.74 0.0002                                                                        | 0.43 0.002                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.70 <0.00001                                                                                                              | 0.65 <0.00001                                                  | 0.6               |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                        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|                                                                                                                            |                                                                                                                                                                                                | Standard error of estimate                                                          | 2.06          | 2.97                                                                                                                      | 3.20                                                                               | 5.51                                                                                                                                                                                                                                                                                                                                                                              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|                                                                                                                            |                                                                                                                                                                                                | Number of qualifying measures in model                                              | 14            | 10                                                                                                                        | 16                                                                                 | 7                                                                                                                                                                                                                                                                                                                                                                                 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| Upper-limb visuomotor measures only                                                                                        |                                                                                                                                                                                                | Adjusted R <sup>2</sup>                                                             | 0.20 0.02     | 0.22 0.02                                                                                                                 | 0.08 0.05                                                                          | 0.13 0.13                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.49 0.0003                                                                                                                | 0.20 0.03                                                      | 0                 |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                        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|                                                                                                                            |                                                                                                                                                                                                | Standard error of estimate                                                          | 4.35          | 4.48                                                                                                                      | 7.42                                                                               | 6.66                                                                                                                                                                                                                                                                                                                                                                              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|                                                                                                                            |                                                                                                                                                                                                | Number of qualifying measures in model                                              | 3             | 4                                                                                                                         | 1                                                                                  | 7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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| Combined eye and arm motor measures (saccades, oculomotor smooth pursuit, upper-limb)                                      |                                                                                                                                                                                                | Adjusted R <sup>2</sup>                                                             | 0.85 <0.00001 | 0.85 <0.00001                                                                                                             | 0.89 <0.00001                                                                      | 0.73 0.00005                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.86 <0.00001                                                                                                              | 0.81 <0.00001                                                  | 0                 |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                         |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |            |           |           |           |           |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                       |  |                         |               |               |              |               |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |   |   |   |   |   |   |  |  |  |
|                                                                                                                            |                                                                                                                                                                                                | Standard error of estimate                                                          | 1.72          | 2.06                                                                                                                      | 2.17                                                                               | 3.83                                                                                                                                                                                                                                                                                                                                                                              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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |            |           |           |           |           |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                       |  |                         |               |               |              |               |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |   |   |   |   |   |   |  |  |  |
|                                                                                                                            |                                                                                                                                                                                                | Number of qualifying measures in model                                              | 12            | 15                                                                                                                        | 12                                                                                 | 13                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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| Neuropsychological measures                                                                                                |                                                                                                                                                                                                | Adjusted R <sup>2</sup>                                                             | 0.32 0.003    | 0.28 0.01                                                                                                                 | 0.13 0.08                                                                          | 0.24 0.02                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.22 0.02                                                                                                                  | 0.17 0.03                                                      | 0                 |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                         |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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|                                                                                                                            |                                                                                                                                                                                                | Standard error of estimate                                                          | 4.07          | 4.38                                                                                                                      | 7.32                                                                               | 6.31                                                                                                                                                                                                                                                                                                                                                                              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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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|                                                                                                                            |                                                                                                                                                                                                | Number of qualifying measures in model                                              | 4             | 6                                                                                                                         | 4                                                                                  | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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| Health status measures (all items SF-36, RPSQ, RHIFQ)                                                                      |                                                                                                                                                                                                | Adjusted R <sup>2</sup>                                                             | 0.79 <0.00001 | 0.70 <0.00001                                                                                                             | 0.54 0.00001                                                                       | 0.69 <0.00001                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 0.70 <0.00001                                                                                                              | 0.68 <0.00001                                                  | 0                 |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                         |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |            |           |           |           |           |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                       |  |                         |               |               |              |               |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |   |   |   |   |   |   |  |  |  |
|                                                                                                                            |                                                                                                                                                                                                | Standard error of estimate                                                          | 2.25          | 2.78                                                                                                                      | 5.24                                                                               | 3.95                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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|                                                                                                                            |                                                                                                                                                                                                | Number of qualifying measures in model                                              | 16            | 8                                                                                                                         | 4                                                                                  | 9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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 |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |      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| 7 <sup>7</sup>                                                                                                             | Christchurch Hospital<br><br>Closed head injury patients GCS, score of between 13 and 15 on first assessment, without falling below 13 at any consecutive assessment at the hospital.          | Matched cohort study<br><br>37 mTBI patients matched to 37 non-head injury controls |               | SF-36 Health Survey (version 2) (SF-36, 8 functional scales and two summary scores),                                      | Patient s assesse d within 1 week of injury (mean 5.5 ±                            | As above but more detail                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | As above same FUp rate in controls                                                                                         | As above same FUp rate in controls                             | 10                |  |  |  |  |  |  |  |                          |  |                                                                               |  |  |  |  |  |  |  |  |  |                        |  |                      |  |                      |  |  |  |  |  |          |          |          |          |          |          |  |  |  |  |         |         |         |         |         |         |  |  |               |  |                         |               |              |             |            |               |               |     |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |   |   |   |   |                                     |  |                         |           |           |           |           |             |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                                                       |  |                         |               |               |               |              |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |    |    |    |    |    |   |                             |  |                         |            |           |           |           |           |           |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |   |   |   |   |   |   |   |                                                       |  |                         |               |               |              |               |               |               |   |  |  |                            |      |      |      |      |      |      |   |  |  |                                        |    |   |   |   |   |   |   |  |  |  |

| Reference                                 | Population                               | Study Design          |          | Outcomes                                                                                                         | Time points and factors                                     | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|                                           | Same population as above                 |                       |          | the Rivermead Postconcussion Symptoms Questionnaire (RPSQ) Rivermead Head Injury Follow-up Questionnaire (RHIFQ) | 3.0 days) and then at 3 months (90 ± 5.5 days) and 6 months | <div>Table 1. Frequency of symptoms/problems on Rivermead Post-Concussion Symptoms Questionnaire (RPSQ) and Rivermead Head-Injury Follow-up Questionnaire (RHIFQ) throughout the first year</div> <table><tr><th rowspan="3">Symptom / problem</th><th colspan="8">Patients reporting symptoms/problems (%)</th><th rowspan="3">Controls (%)</th></tr><tr><th colspan="2">1 week</th><th colspan="2">3 months</th><th colspan="2">6 months</th><th colspan="2">12 months</th></tr><tr><th>Overall</th><th>Score of 2 or higher*</th><th>Overall</th><th>Score of 2 or higher*</th><th>Overall</th><th>Score of 2 or higher*</th><th>Overall</th><th>Score of 2 or higher*</th></tr><tr><td colspan="10"><i>RPSQ</i></td></tr><tr><td>Fatigue/tiring more easily</td><td>89</td><td>76</td><td>59</td><td>27</td><td>59</td><td>22</td><td>55</td><td>26</td><td>22</td></tr><tr><td>Headaches</td><td>86</td><td>68</td><td>46</td><td>14</td><td>46</td><td>22</td><td>52</td><td>26</td><td>24</td></tr><tr><td>Dizziness</td><td>84</td><td>43</td><td>35</td><td>16</td><td>41</td><td>19</td><td>39</td><td>23</td><td>22</td></tr><tr><td>Poor concentration</td><td>84</td><td>59</td><td>62</td><td>32</td><td>59</td><td>27</td><td>58</td><td>26</td><td>35</td></tr><tr><td>Taking longer to think</td><td>81</td><td>54</td><td>49</td><td>16</td><td>49</td><td>16</td><td>45</td><td>16</td><td>24</td></tr><tr><td>Forgetfulness/poor memory</td><td>76</td><td>41</td><td>51</td><td>27</td><td>54</td><td>27</td><td>61</td><td>16</td><td>24</td></tr><tr><td>Restlessness</td><td>65</td><td>30</td><td>41</td><td>11</td><td>43</td><td>14</td><td>35</td><td>3</td><td>30</td></tr><tr><td>Frustration/Impatience</td><td>62</td><td>24</td><td>43</td><td>19</td><td>57</td><td>16</td><td>35</td><td>16</td><td>35</td></tr><tr><td>Irritability/easily angered</td><td>59</td><td>35</td><td>46</td><td>19</td><td>51</td><td>22</td><td>42</td><td>13</td><td>32</td></tr><tr><td>Sleep disturbance</td><td>57</td><td>41</td><td>43</td><td>22</td><td>46</td><td>14</td><td>39</td><td>19</td><td>43</td></tr><tr><td>Light sensitivity</td><td>54</td><td>35</td><td>19</td><td>8</td><td>16</td><td>11</td><td>32</td><td>6</td><td>14</td></tr><tr><td>Noise sensitivity</td><td>49</td><td>30</td><td>32</td><td>14</td><td>32</td><td>16</td><td>29</td><td>13</td><td>11</td></tr><tr><td>Feeling depressed</td><td>49</td><td>14</td><td>27</td><td>11</td><td>38</td><td>11</td><td>32</td><td>19</td><td>16</td></tr><tr><td>Blurred vision</td><td>46</td><td>32</td><td>19</td><td>8</td><td>24</td><td>16</td><td>39</td><td>23</td><td>16</td></tr><tr><td>Nausea/vomiting</td><td>30</td><td>14</td><td>5</td><td>3</td><td>8</td><td>5</td><td>10</td><td>3</td><td>11</td></tr><tr><td>Double vision</td><td>19</td><td>14</td><td>14</td><td>5</td><td>16</td><td>11</td><td>19</td><td>6</td><td>0</td></tr><tr><td colspan="10"><i>RHIFQ</i></td></tr><tr><td>Finding work more tiring</td><td>86</td><td>73</td><td>41</td><td>8</td><td>41</td><td>14</td><td>35</td><td>23</td><td>-</td></tr><tr><td>Maintaining previous work load</td><td>84</td><td>65</td><td>38</td><td>8</td><td>32</td><td>14</td><td>19</td><td>10</td><td>-</td></tr><tr><td>Enjoying previous leisure activities</td><td>78</td><td>70</td><td>16</td><td>8</td><td>14</td><td>8</td><td>10</td><td>6</td><td>-</td></tr><tr><td>Routine domestic activities</td><td>65</td><td>46</td><td>8</td><td>3</td><td>8</td><td>5</td><td>10</td><td>3</td><td>-</td></tr><tr><td>Participation in previous social activity</td><td>65</td><td>41</td><td>11</td><td>3</td><td>11</td><td>5</td><td>3</td><td>3</td><td>-</td></tr><tr><td>Coping with family demands</td><td>62</td><td>27</td><td>27</td><td>5</td><td>19</td><td>8</td><td>19</td><td>10</td><td>-</td></tr><tr><td>Conversation with 2 or more</td><td>49</td><td>8</td><td>16</td><td>5</td><td>14</td><td>5</td><td>13</td><td>10</td><td>-</td></tr><tr><td>Conversation with 1 person</td><td>41</td><td>8</td><td>11</td><td>5</td><td>11</td><td>5</td><td>6</td><td>6</td><td>-</td></tr><tr><td>Relationships with previous friends</td><td>27</td><td>11</td><td>11</td><td>3</td><td>8</td><td>5</td><td>3</td><td>3</td><td>-</td></tr><tr><td>Relationship with partner</td><td>24</td><td>8</td><td>8</td><td>3</td><td>3</td><td>3</td><td>6</td><td>6</td><td>-</td></tr></table> <div>*"Score of 2 or higher" = subjects who reported a score of 2, 3 or 4 for this symptom (scale = 0-4), i.e. the symptom was at least a mild problem</div> | Symptom / problem                                                | Patients reporting symptoms/problems (%)                       |                   |  |  |  |  |  |  | Controls (%) | 1 week |  | 3 months |  | 6 months |  | 12 months |  | Overall | Score of 2 or higher* | Overall | Score of 2 or higher* | Overall | Score of 2 or higher* | Overall | Score of 2 or higher* | <i>RPSQ</i> |  |  |  |  |  |  |  |  |  | Fatigue/tiring more easily | 89 | 76 | 59 | 27 | 59 | 22 | 55 | 26 | 22 | Headaches | 86 | 68 | 46 | 14 | 46 | 22 | 52 | 26 | 24 | Dizziness | 84 | 43 | 35 | 16 | 41 | 19 | 39 | 23 | 22 | Poor concentration | 84 | 59 | 62 | 32 | 59 | 27 | 58 | 26 | 35 | Taking longer to think | 81 | 54 | 49 | 16 | 49 | 16 | 45 | 16 | 24 | Forgetfulness/poor memory | 76 | 41 | 51 | 27 | 54 | 27 | 61 | 16 | 24 | Restlessness | 65 | 30 | 41 | 11 | 43 | 14 | 35 | 3 | 30 | Frustration/Impatience | 62 | 24 | 43 | 19 | 57 | 16 | 35 | 16 | 35 | Irritability/easily angered | 59 | 35 | 46 | 19 | 51 | 22 | 42 | 13 | 32 | Sleep disturbance | 57 | 41 | 43 | 22 | 46 | 14 | 39 | 19 | 43 | Light sensitivity | 54 | 35 | 19 | 8 | 16 | 11 | 32 | 6 | 14 | Noise sensitivity | 49 | 30 | 32 | 14 | 32 | 16 | 29 | 13 | 11 | Feeling depressed | 49 | 14 | 27 | 11 | 38 | 11 | 32 | 19 | 16 | Blurred vision | 46 | 32 | 19 | 8 | 24 | 16 | 39 | 23 | 16 | Nausea/vomiting | 30 | 14 | 5 | 3 | 8 | 5 | 10 | 3 | 11 | Double vision | 19 | 14 | 14 | 5 | 16 | 11 | 19 | 6 | 0 | <i>RHIFQ</i> |  |  |  |  |  |  |  |  |  | Finding work more tiring | 86 | 73 | 41 | 8 | 41 | 14 | 35 | 23 | - | Maintaining previous work load | 84 | 65 | 38 | 8 | 32 | 14 | 19 | 10 | - | Enjoying previous leisure activities | 78 | 70 | 16 | 8 | 14 | 8 | 10 | 6 | - | Routine domestic activities | 65 | 46 | 8 | 3 | 8 | 5 | 10 | 3 | - | Participation in previous social activity | 65 | 41 | 11 | 3 | 11 | 5 | 3 | 3 | - | Coping with family demands | 62 | 27 | 27 | 5 | 19 | 8 | 19 | 10 | - | Conversation with 2 or more | 49 | 8 | 16 | 5 | 14 | 5 | 13 | 10 | - | Conversation with 1 person | 41 | 8 | 11 | 5 | 11 | 5 | 6 | 6 | - | Relationships with previous friends | 27 | 11 | 11 | 3 | 8 | 5 | 3 | 3 | - | Relationship with partner | 24 | 8 | 8 | 3 | 3 | 3 | 6 | 6 | - |  |  |  |
| Symptom / problem                         | Patients reporting symptoms/problems (%) |                       |          |                                                                                                                  |                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|
|                                           | 1 week                                   |                       | 3 months |                                                                                                                  | 6 months                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|
|                                           | Overall                                  | Score of 2 or higher* | Overall  | Score of 2 or higher*                                                                                            | Overall                                                     | Score of 2 or higher*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| <i>RPSQ</i>                               |                                          |                       |          |                                                                                                                  |                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|
| Fatigue/tiring more easily                | 89                                       | 76                    | 59       | 27                                                                                                               | 59                                                          | 22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Headaches                                 | 86                                       | 68                    | 46       | 14                                                                                                               | 46                                                          | 22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Dizziness                                 | 84                                       | 43                    | 35       | 16                                                                                                               | 41                                                          | 19                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Poor concentration                        | 84                                       | 59                    | 62       | 32                                                                                                               | 59                                                          | 27                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 58                                                               | 26                                                             | 35                |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Taking longer to think                    | 81                                       | 54                    | 49       | 16                                                                                                               | 49                                                          | 16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Forgetfulness/poor memory                 | 76                                       | 41                    | 51       | 27                                                                                                               | 54                                                          | 27                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Restlessness                              | 65                                       | 30                    | 41       | 11                                                                                                               | 43                                                          | 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Frustration/Impatience                    | 62                                       | 24                    | 43       | 19                                                                                                               | 57                                                          | 16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 35                                                               | 16                                                             | 35                |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Irritability/easily angered               | 59                                       | 35                    | 46       | 19                                                                                                               | 51                                                          | 22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 42                                                               | 13                                                             | 32                |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Sleep disturbance                         | 57                                       | 41                    | 43       | 22                                                                                                               | 46                                                          | 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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|
| Light sensitivity                         | 54                                       | 35                    | 19       | 8                                                                                                                | 16                                                          | 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Noise sensitivity                         | 49                                       | 30                    | 32       | 14                                                                                                               | 32                                                          | 16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Feeling depressed                         | 49                                       | 14                    | 27       | 11                                                                                                               | 38                                                          | 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Blurred vision                            | 46                                       | 32                    | 19       | 8                                                                                                                | 24                                                          | 16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Nausea/vomiting                           | 30                                       | 14                    | 5        | 3                                                                                                                | 8                                                           | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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|
| Double vision                             | 19                                       | 14                    | 14       | 5                                                                                                                | 16                                                          | 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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    |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |  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| <i>RHIFQ</i>                              |                                          |                       |          |                                                                                                                  |                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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|
| Finding work more tiring                  | 86                                       | 73                    | 41       | 8                                                                                                                | 41                                                          | 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 35                                                               | 23                                                             | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Maintaining previous work load            | 84                                       | 65                    | 38       | 8                                                                                                                | 32                                                          | 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 19                                                               | 10                                                             | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Enjoying previous leisure activities      | 78                                       | 70                    | 16       | 8                                                                                                                | 14                                                          | 8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 10                                                               | 6                                                              | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Routine domestic activities               | 65                                       | 46                    | 8        | 3                                                                                                                | 8                                                           | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 10                                                               | 3                                                              | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Participation in previous social activity | 65                                       | 41                    | 11       | 3                                                                                                                | 11                                                          | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 3                                                                | 3                                                              | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Coping with family demands                | 62                                       | 27                    | 27       | 5                                                                                                                | 19                                                          | 8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 19                                                               | 10                                                             | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Conversation with 2 or more               | 49                                       | 8                     | 16       | 5                                                                                                                | 14                                                          | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 13                                                               | 10                                                             | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Conversation with 1 person                | 41                                       | 8                     | 11       | 5                                                                                                                | 11                                                          | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 6                                                                | 6                                                              | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Relationships with previous friends       | 27                                       | 11                    | 11       | 3                                                                                                                | 8                                                           | 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 3                                                                | 3                                                              | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |
| Relationship with partner                 | 24                                       | 8                     | 8        | 3                                                                                                                | 3                                                           | 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 6                                                                | 6                                                              | -                 |  |  |  |  |  |  |              |        |  |          |  |          |  |           |  |         |                       |         |                       |         |                       |         |                       |             |  |  |  |  |  |  |  |  |  |                            |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |           |    |    |    |    |    |    |    |    |    |                    |    |    |    |    |    |    |    |    |    |                        |    |    |    |    |    |    |    |    |    |                           |    |    |    |    |    |    |    |    |    |              |    |    |    |    |    |    |    |   |    |                        |    |    |    |    |    |    |    |    |    |                             |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |   |    |    |    |   |    |                   |    |    |    |    |    |    |    |    |    |                   |    |    |    |    |    |    |    |    |    |                |    |    |    |   |    |    |    |    |    |                 |    |    |   |   |   |   |    |   |    |               |    |    |    |   |    |    |    |   |   |              |  |  |  |  |  |  |  |  |  |                          |    |    |    |   |    |    |    |    |   |                                |    |    |    |   |    |    |    |    |   |                                      |    |    |    |   |    |   |    |   |   |                             |    |    |   |   |   |   |    |   |   |                                           |    |    |    |   |    |   |   |   |   |                            |    |    |    |   |    |   |    |    |   |                             |    |   |    |   |    |   |    |    |   |                            |    |   |    |   |    |   |   |   |   |                                     |    |    |    |   |   |   |   |   |   |                           |    |   |   |   |   |   |   |   |   |  |  |  |

| Reference              | Population                                                                                                                                                                        | Study Design             |                         | Outcomes                                                | Time points and factors                                              | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      | 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|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-------------------------|---------------------------------------------------------|----------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|--|--|--|--|--|--|--------|--|----------|--|----------|--|-----------|--|------------------------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|---------------------|--------|--|------|--|------|--|------|--|-----|-------|-------|----|------|-------|----|------|-------|-----------|-------|-------|--|--|--|--|----|------|----------------------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|---------------------|------|--|------|--|------|--|------|--|-----------|-------|-------|-----------|-------|-------|----|------|-------|-----|------|-------|--|--|--|--|----|------|----|------|-------|--|--|--|--|--|--|----------------|-------|-------|--|--|--|--|--|--|------|---|---|-------------------------|------|-------------------------|------|-------------------------|------|---------------------|--|--|------|--|------|--|------|--|-----------------------|--|--|----|-------|-------|----|-------|-------|--|--|--|--|--|-----|-------|-------|-------|-------|---|---|-------------------------|------|-------------------------|-------|-------------------------|------|---------------------|--|--|-----------------------|--|------|--|------|--|-----------------------|--|--|--|--|----|-------|-------|----|--|--|--|--|--|--|--|--|-------|--|--|--|
|                        |                                                                                                                                                                                   |                          |                         |                                                         |                                                                      | <div>Table III. Associations of age, IQ, years of education and measures of injury severity with the Rivermead Post-Concussion Symptoms Questionnaire (RPSQ), Rivermead Head-Injury Follow-up Questionnaire (RHIFQ) and Short-Form 36 Health Survey (SF-36)</div> <table><thead><tr><th rowspan="2">Dependent measures</th><th colspan="8">Time delay post-injury</th></tr><tr><th colspan="2">1 week</th><th colspan="2">3 months</th><th colspan="2">6 months</th><th colspan="2">12 months</th></tr></thead><tbody><tr><td>SF-36 Physical Summary</td><td>Adjusted R<sup>2</sup></td><td>0.16</td><td>Adjusted R<sup>2</sup></td><td>0.19</td><td>Adjusted R<sup>2</sup></td><td>0.11</td><td>Adjusted R<sup>2</sup></td><td>0.10</td></tr><tr><td>In-model variables*</td><td>Beta**</td><td></td><td>Beta</td><td></td><td>Beta</td><td></td><td>Beta</td><td></td></tr><tr><td>PTA</td><td>-0.47</td><td>0.012</td><td>IQ</td><td>0.46</td><td>0.008</td><td>IQ</td><td>0.37</td><td>0.038</td></tr><tr><td>GCS score</td><td>-0.28</td><td>0.123</td><td></td><td></td><td></td><td></td><td>IQ</td><td>0.37</td></tr><tr><td>SF-36 Mental Summary</td><td>Adjusted R<sup>2</sup></td><td>0.32</td><td>Adjusted R<sup>2</sup></td><td>0.08</td><td>Adjusted R<sup>2</sup></td><td>0.07</td><td>Adjusted R<sup>2</sup></td><td>0.12</td></tr><tr><td>In-model variables*</td><td>Beta</td><td></td><td>Beta</td><td></td><td>Beta</td><td></td><td>Beta</td><td></td></tr><tr><td>GCS score</td><td>-0.42</td><td>0.010</td><td>GCS score</td><td>-0.33</td><td>0.064</td><td>IQ</td><td>0.32</td><td>0.075</td></tr><tr><td>Age</td><td>0.30</td><td>0.054</td><td></td><td></td><td></td><td></td><td>IQ</td><td>0.40</td></tr><tr><td>IQ</td><td>0.42</td><td>0.023</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Years of educ.</td><td>-0.36</td><td>0.052</td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>RPSQ</td><td>-</td><td>-</td><td>Adjusted R<sup>2</sup></td><td>0.12</td><td>Adjusted R<sup>2</sup></td><td>0.08</td><td>Adjusted R<sup>2</sup></td><td>0.14</td></tr><tr><td>In-model variables*</td><td></td><td></td><td>Beta</td><td></td><td>Beta</td><td></td><td>Beta</td><td></td></tr><tr><td>No variables in model</td><td></td><td></td><td>IQ</td><td>-0.38</td><td>0.030</td><td>IQ</td><td>-0.31</td><td>0.085</td></tr><tr><td></td><td></td><td></td><td></td><td></td><td>LOC</td><td>-0.26</td><td>0.140</td><td>-0.42</td></tr><tr><td>RHIFQ</td><td>-</td><td>-</td><td>Adjusted R<sup>2</sup></td><td>0.11</td><td>Adjusted R<sup>2</sup></td><td>0.034</td><td>Adjusted R<sup>2</sup></td><td>0.08</td></tr><tr><td>In-model variables*</td><td></td><td></td><td>No variables in model</td><td></td><td>Beta</td><td></td><td>Beta</td><td></td></tr><tr><td>No variables in model</td><td></td><td></td><td></td><td></td><td>IQ</td><td>-0.38</td><td>0.034</td><td>IQ</td></tr><tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>-0.34</td></tr></tbody></table> <div>*In-model variables = all independent variables that make unique, non-redundant contributions to explaining variance in the dependent measure.<br/>**Beta = standardized regression coefficients for in-model variables.<br/>PTA: post-traumatic amnesia; GCS: Glasgow Coma Scale; LOC: loss of consciousness.</div> | Dependent measures                                               | Time delay post-injury                                         |                   |  |  |  |  |  |  | 1 week |  | 3 months |  | 6 months |  | 12 months |  | SF-36 Physical Summary | Adjusted R <sup>2</sup> | 0.16 | Adjusted R <sup>2</sup> | 0.19 | Adjusted R <sup>2</sup> | 0.11 | Adjusted R <sup>2</sup> | 0.10 | In-model variables* | Beta** |  | Beta |  | Beta |  | Beta |  | PTA | -0.47 | 0.012 | IQ | 0.46 | 0.008 | IQ | 0.37 | 0.038 | GCS score | -0.28 | 0.123 |  |  |  |  | IQ | 0.37 | SF-36 Mental Summary | Adjusted R <sup>2</sup> | 0.32 | Adjusted R <sup>2</sup> | 0.08 | Adjusted R <sup>2</sup> | 0.07 | Adjusted R <sup>2</sup> | 0.12 | In-model variables* | Beta |  | Beta |  | Beta |  | Beta |  | GCS score | -0.42 | 0.010 | GCS score | -0.33 | 0.064 | IQ | 0.32 | 0.075 | Age | 0.30 | 0.054 |  |  |  |  | IQ | 0.40 | IQ | 0.42 | 0.023 |  |  |  |  |  |  | Years of educ. | -0.36 | 0.052 |  |  |  |  |  |  | RPSQ | - | - | Adjusted R <sup>2</sup> | 0.12 | Adjusted R <sup>2</sup> | 0.08 | Adjusted R <sup>2</sup> | 0.14 | In-model variables* |  |  | Beta |  | Beta |  | Beta |  | No variables in model |  |  | IQ | -0.38 | 0.030 | IQ | -0.31 | 0.085 |  |  |  |  |  | LOC | -0.26 | 0.140 | -0.42 | RHIFQ | - | - | Adjusted R <sup>2</sup> | 0.11 | Adjusted R <sup>2</sup> | 0.034 | Adjusted R <sup>2</sup> | 0.08 | In-model variables* |  |  | No variables in model |  | Beta |  | Beta |  | No variables in model |  |  |  |  | IQ | -0.38 | 0.034 | IQ |  |  |  |  |  |  |  |  | -0.34 |  |  |  |
| Dependent measures     | Time delay post-injury                                                                                                                                                            |                          |                         |                                                         |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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|                        | 1 week                                                                                                                                                                            |                          | 3 months                |                                                         | 6 months                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| SF-36 Physical Summary | Adjusted R <sup>2</sup>                                                                                                                                                           | 0.16                     | Adjusted R <sup>2</sup> | 0.19                                                    | Adjusted R <sup>2</sup>                                              | 0.11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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                |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      | 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| In-model variables*    | Beta**                                                                                                                                                                            |                          | Beta                    |                                                         | Beta                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| PTA                    | -0.47                                                                                                                                                                             | 0.012                    | IQ                      | 0.46                                                    | 0.008                                                                | IQ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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                |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| GCS score              | -0.28                                                                                                                                                                             | 0.123                    |                         |                                                         |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| SF-36 Mental Summary   | Adjusted R <sup>2</sup>                                                                                                                                                           | 0.32                     | Adjusted R <sup>2</sup> | 0.08                                                    | Adjusted R <sup>2</sup>                                              | 0.07                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Adjusted R <sup>2</sup>                                          | 0.12                                                           |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| In-model variables*    | Beta                                                                                                                                                                              |                          | Beta                    |                                                         | Beta                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                        |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| GCS score              | -0.42                                                                                                                                                                             | 0.010                    | GCS score               | -0.33                                                   | 0.064                                                                | IQ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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                |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| Age                    | 0.30                                                                                                                                                                              | 0.054                    |                         |                                                         |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| IQ                     | 0.42                                                                                                                                                                              | 0.023                    |                         |                                                         |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                        |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| Years of educ.         | -0.36                                                                                                                                                                             | 0.052                    |                         |                                                         |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                        |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| RPSQ                   | -                                                                                                                                                                                 | -                        | Adjusted R <sup>2</sup> | 0.12                                                    | Adjusted R <sup>2</sup>                                              | 0.08                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Adjusted R <sup>2</sup>                                          | 0.14                                                           |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| In-model variables*    |                                                                                                                                                                                   |                          | Beta                    |                                                         | Beta                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                        |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| No variables in model  |                                                                                                                                                                                   |                          | IQ                      | -0.38                                                   | 0.030                                                                | IQ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | -0.31                                                            | 0.085                                                          |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
|                        |                                                                                                                                                                                   |                          |                         |                                                         | LOC                                                                  | -0.26                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.140                                                            | -0.42                                                          |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| RHIFQ                  | -                                                                                                                                                                                 | -                        | Adjusted R <sup>2</sup> | 0.11                                                    | Adjusted R <sup>2</sup>                                              | 0.034                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Adjusted R <sup>2</sup>                                          | 0.08                                                           |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| In-model variables*    |                                                                                                                                                                                   |                          | No variables in model   |                                                         | Beta                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| No variables in model  |                                                                                                                                                                                   |                          |                         |                                                         | IQ                                                                   | -0.38                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0.034                                                            | IQ                                                             |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
|                        |                                                                                                                                                                                   |                          |                         |                                                         |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                  | -0.34                                                          |                   |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |
| 8 <sup>a</sup>         | 16 -60 year olds with mTBI (WHO criteria) patients recruited from a regional level 1 trauma centre and Municipal Emergency clinic in Trondheim, Norway (April 2014–December 2015) | Prospective cohort study |                         | Rivermead Post Concussion Symptoms Questionnaire (RPSQ) | Telephone interview at 2 weeks, 3 months and 12 months after injury, | RPSQ symptom prevalence (mean score SD)<br><br>2 weeks 50% (9.8 ± 10.9)<br><br>3 months 25.5% ( 6.4± 9.3),<br><br>12 months 19.1% ( 5.1 ± 8.5) .                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 86% of 379                                                       | 87% at 12 months                                               | 12                |  |  |  |  |  |  |        |  |          |  |          |  |           |  |                        |                         |      |                         |      |                         |      |                         |      |                     |        |  |      |  |      |  |      |  |     |       |       |    |      |       |    |      |       |           |       |       |  |  |  |  |    |      |                      |                         |      |                         |      |                         |      |                         |      |                     |      |  |      |  |      |  |      |  |           |       |       |           |       |       |    |      |       |     |      |       |  |  |  |  |    |      |    |      |       |  |  |  |  |  |  |                |       |       |  |  |  |  |  |  |      |   |   |                         |      |                         |      |                         |      |                     |  |  |      |  |      |  |      |  |                       |  |  |    |       |       |    |       |       |  |  |  |  |  |     |       |       |       |       |   |   |                         |      |                         |       |                         |      |                     |  |  |                       |  |      |  |      |  |                       |  |  |  |  |    |       |       |    |  |  |  |  |  |  |  |  |       |  |  |  |

| Refere<br>nce  | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Study Design                                                                                       |      | Outcomes                                                            | Time<br>points<br>and<br>factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |      |        |      |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
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| 9 <sup>9</sup> | <p>Traumatically injured patients recruited at 2 ED in California, USA. mTBI defined as a patient, aged 18–64 years inclusive with a head injury from a blow or impact to the head</p> <p>Including acceleration/deceleration exposures that resulted in: evidence of transient confusion or disorientation, memory dysfunction, loss of consciousness</p> <p>less than 30 minutes or Glasgow Coma Score (GCS) of 13, 14 or 15.</p> <p>The comparison non-mTBI cohort</p> <p>must not have had a head trauma a 1 year before have had an Injury Severity Score (ISS) similar to enrolled mTBI patients. <a href="#">maximum head Abbreviated Injury Scale(AIS) for study eligibility was a 1 or 2 for all MTBI patients.</a></p> <p><a href="#">Inability to give informed consent, non-English or</a></p> | Prospective longitudinal cohort study of mTBI patents compared to non-head injury trauma patients. |      | <p>Rivermead Post-Concussion Symptom</p> <p>Questionnaire (RPQ)</p> | 3 and 6 months post-injury       | <p>Base (n = 2005) 3 months (n = 1129) 6 months (n = 995)?ratio of mTBI to controls</p> <p>Table III. Mean Rivermead Post-Concussion Symptoms Questionnaire (RPQ) scores for patients in MTBI and Comparison injury c<br/>gender, at 3 and 6 months post-injury.</p> <table><tr><th rowspan="3">Age group</th><th colspan="6">3 Months post-injury</th><th colspan="6">6 Months post-injury</th></tr><tr><th colspan="3">MTBI</th><th colspan="3">Comparison</th><th colspan="3">MTBI</th><th colspan="3">Co</th></tr><tr><th>Male</th><th>Female</th><th>Both</th><th>Male</th><th>Female</th><th>Both</th><th>Male</th><th>Female</th><th>Both</th><th>Male</th><th>Female</th><th>Both</th></tr><tr><td>18–34</td><td>5.61</td><td>9.06</td><td>6.82</td><td>2.95</td><td>4.93</td><td>3.60</td><td>4.37</td><td>8.24</td><td>5.72</td><td>3.08</td><td>5.72</td><td>3.08</td></tr><tr><td>35–54</td><td>6.16</td><td>10.57</td><td>7.80</td><td>3.32</td><td>5.85</td><td>4.42</td><td>4.05</td><td>8.49</td><td>5.75</td><td>2.20</td><td>5.75</td><td>2.20</td></tr><tr><td>55–64</td><td>5.86</td><td>10.17</td><td>7.80</td><td>2.65</td><td>7.22</td><td>4.60</td><td>6.74</td><td>10.33</td><td>8.32</td><td>3.69</td><td>8.32</td><td>3.69</td></tr><tr><td>All ages</td><td>5.82</td><td>9.72</td><td>7.26</td><td>3.06</td><td>5.62</td><td>4.03</td><td>4.45</td><td>8.57</td><td>5.97</td><td>2.84</td><td>5.97</td><td>2.84</td></tr></table> | Age group                                                                    | 3 Months post-injury                                                    |                      |      |        |      |  | 6 Months post-injury |  |  |  |  |  | MTBI |  |  | Comparison |  |  | MTBI |  |  | Co |  |  | Male | Female | Both | Male | Female | Both | Male | Female | Both | Male | Female | Both | 18–34 | 5.61 | 9.06 | 6.82 | 2.95 | 4.93 | 3.60 | 4.37 | 8.24 | 5.72 | 3.08 | 5.72 | 3.08 | 35–54 | 6.16 | 10.57 | 7.80 | 3.32 | 5.85 | 4.42 | 4.05 | 8.49 | 5.75 | 2.20 | 5.75 | 2.20 | 55–64 | 5.86 | 10.17 | 7.80 | 2.65 | 7.22 | 4.60 | 6.74 | 10.33 | 8.32 | 3.69 | 8.32 | 3.69 | All ages | 5.82 | 9.72 | 7.26 | 3.06 | 5.62 | 4.03 | 4.45 | 8.57 | 5.97 | 2.84 | 5.97 | 2.84 | 56% of 2005 overall for cases and non TBI injured controls | 6 month 81% cases 75% controls | 13 |
| Age group      | 3 Months post-injury                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                    |      |                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                              | 6 Months post-injury                                                    |                      |      |        |      |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
|                | MTBI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                    |      | Comparison                                                          |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                              | MTBI                                                                    |                      |      | Co     |      |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
|                | Male                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Female                                                                                             | Both | Male                                                                | Female                           | Both                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Male                                                                         | Female                                                                  | Both                 | Male | Female | Both |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
| 18–34          | 5.61                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 9.06                                                                                               | 6.82 | 2.95                                                                | 4.93                             | 3.60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 4.37                                                                         | 8.24                                                                    | 5.72                 | 3.08 | 5.72   | 3.08 |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
| 35–54          | 6.16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 10.57                                                                                              | 7.80 | 3.32                                                                | 5.85                             | 4.42                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 4.05                                                                         | 8.49                                                                    | 5.75                 | 2.20 | 5.75   | 2.20 |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
| 55–64          | 5.86                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 10.17                                                                                              | 7.80 | 2.65                                                                | 7.22                             | 4.60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 6.74                                                                         | 10.33                                                                   | 8.32                 | 3.69 | 8.32   | 3.69 |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |
| All ages       | 5.82                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 9.72                                                                                               | 7.26 | 3.06                                                                | 5.62                             | 4.03                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 4.45                                                                         | 8.57                                                                    | 5.97                 | 2.84 | 5.97   | 2.84 |  |                      |  |  |  |  |  |      |  |  |            |  |  |      |  |  |    |  |  |      |        |      |      |        |      |      |        |      |      |        |      |       |      |      |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |      |      |      |      |      |       |      |       |      |      |      |      |      |       |      |      |      |      |          |      |      |      |      |      |      |      |      |      |      |      |      |                                                            |                                |    |

| Reference                           | Population                                                                                                                                       | Study Design             |       | Outcomes          | Time points and factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |         |  |  |  |                   |  |  |  |          |  |                    |  |                   |  |         |                    |  |                   |  |     |                  |    |       |    |       |      |    |       |    |       |        |      |    |     |    |     |      |    |     |    |     |        |    |     |    |     |    |     |    |     |      |           |    |     |    |     |      |    |     |    |     |                             |    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|                                     | <a href="#">SpanishspeakingSpanish speaking</a>                                                                                                  |                          |       |                   |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| 10 <sup>10</sup>                    | Three level 1 trauma centres USA. ≥18 years<br><br>with ED admission GCS 13–15, without evidence of intracranial injury on ED admission head CT. | Prospective Cohort Study |       | GOSE              | 3 and 6 months          | 271 included in analysis<br><br>211 completed 3-month outcomes and 185 completed 6-month outcomes.<br><table><thead><tr><th colspan="2"></th><th colspan="4">3 Months, n = 211</th><th></th><th colspan="4">6 Months, n = 185</th></tr><tr><th colspan="2">Variable</th><th colspan="2">GOSE &lt; 8 (n = 127)</th><th colspan="2">GOSE ≥ 8 (n = 84)</th><th>p-Value</th><th colspan="2">GOSE &lt; 8 (n = 121)</th><th colspan="2">GOSE ≥ 8 (n = 64)</th></tr></thead><tbody><tr><td>Age</td><td>Years (med, IQR)</td><td>40</td><td>26–54</td><td>36</td><td>26–50</td><td>0.30</td><td>40</td><td>26–52</td><td>35</td><td>24–51</td></tr><tr><td rowspan="2">Gender</td><td>Male</td><td>84</td><td>59%</td><td>59</td><td>41%</td><td rowspan="2">0.55</td><td>79</td><td>63%</td><td>46</td><td>37%</td></tr><tr><td>Female</td><td>43</td><td>63%</td><td>25</td><td>37%</td><td>42</td><td>70%</td><td>18</td><td>30%</td></tr><tr><td rowspan="6">Race</td><td>Caucasian</td><td>83</td><td>54%</td><td>72</td><td>46%</td><td rowspan="6">0.02</td><td>80</td><td>60%</td><td>54</td><td>40%</td></tr><tr><td>African American or African</td><td>18</td><td>75%</td><td>6</td><td>25%</td><td>15</td><td>75%</td><td>5</td><td>25%</td></tr><tr><td>Asian</td><td>12</td><td>86%</td><td>2</td><td>14%</td><td>12</td><td>92%</td><td>1</td><td>8%</td></tr><tr><td>American Indian or Alaskan</td><td>2</td><td>100%</td><td>0</td><td>0%</td><td>2</td><td>100%</td><td>0</td><td>0%</td></tr><tr><td>Hawaiian or Pacific Islander</td><td>2</td><td>100%</td><td>0</td><td>0%</td><td>4</td><td>100%</td><td>0</td><td>0%</td></tr><tr><td>More than One Race</td><td>6</td><td>60%</td><td>4</td><td>40%</td><td>7</td><td>64%</td><td>4</td><td>36%</td></tr><tr><td></td><td>Not Available</td><td>1</td><td>100%</td><td>0</td><td>0%</td><td></td><td>1</td><td>100%</td><td>0</td><td>0%</td></tr><tr><td rowspan="2">Ethnicity</td><td>Non-Hispanic</td><td>96</td><td>58%</td><td>70</td><td>42%</td><td rowspan="2">0.23</td><td>91</td><td>61%</td><td>57</td><td>39%</td></tr><tr><td>Hispanic</td><td>31</td><td>69%</td><td>14</td><td>31%</td><td>30</td><td>83%</td><td>7</td><td>19%</td></tr><tr><td>Years of Education</td><td>Years (med, IQR)</td><td>13</td><td>12–16</td><td>15</td><td>12.5–16</td><td>0.006</td><td>14</td><td>12–16</td><td>15</td><td>13–16.5</td></tr><tr><td rowspan="2">Psychiatric History</td><td>No</td><td>72</td><td>53%</td><td>63</td><td>47%</td><td rowspan="2">&lt;0.01</td><td>63</td><td>56%</td><td>50</td><td>44%</td></tr><tr><td>Yes</td><td>55</td><td>72%</td><td>21</td><td>26%</td><td>58</td><td>81%</td><td>14</td><td>19%</td></tr><tr><td rowspan="2">Injury Mechanism</td><td>Fall/Accident/Other</td><td>101</td><td>56%</td><td>78</td><td>44%</td><td rowspan="2">0.01</td><td>95</td><td>62%</td><td>59</td><td>38%</td></tr><tr><td>Assault</td><td>26</td><td>81%</td><td>6</td><td>19%</td><td>26</td><td>84%</td><td>5</td><td>16%</td></tr><tr><td rowspan="3">Glasgow Coma Scale</td><td>13</td><td>5</td><td>71%</td><td>2</td><td>29%</td><td rowspan="3">0.81</td><td>5</td><td>100%</td><td>0</td><td>0%</td></tr><tr><td>14</td><td>28</td><td>62%</td><td>17</td><td>38%</td><td>24</td><td>60%</td><td>16</td><td>40%</td></tr><tr><td>15</td><td>94</td><td>59%</td><td>65</td><td>41%</td><td>92</td><td>66%</td><td>48</td><td>34%</td></tr><tr><td rowspan="2">Anticoagulant Use</td><td>No</td><td>120</td><td>60%</td><td>79</td><td>40%</td><td rowspan="2">&gt;0.99</td><td>112</td><td>63%</td><td>61</td><td>35%</td></tr><tr><td>Yes</td><td>7</td><td>58%</td><td>5</td><td>42%</td><td>9</td><td>75%</td><td>3</td><td>25%</td></tr><tr><td rowspan="4">Loss of consciousness</td><td>None</td><td>39</td><td>61%</td><td>25</td><td>39%</td><td rowspan="4">0.58</td><td>31</td><td>60%</td><td>21</td><td>40%</td></tr><tr><td>&lt; 30 min</td><td>54</td><td>37%</td><td>41</td><td>47%</td><td>59</td><td>69%</td><td>27</td><td>31%</td></tr><tr><td>≥ 30 min</td><td>4</td><td>50%</td><td>4</td><td>50%</td><td>7</td><td>64%</td><td>4</td><td>36%</td></tr><tr><td>Unknown</td><td>30</td><td>68%</td><td>14</td><td>32%</td><td>24</td><td>67%</td><td>12</td><td>33%</td></tr><tr><td rowspan="4">Post-traumatic amnesia</td><td>None</td><td>48</td><td>61%</td><td>31</td><td>39%</td><td rowspan="4">0.66</td><td>45</td><td>63%</td><td>26</td><td>37%</td></tr><tr><td>&lt; 30 min</td><td>41</td><td>56%</td><td>32</td><td>44%</td><td>39</td><td>66%</td><td>13</td><td>34%</td></tr><tr><td>≥ 30 min</td><td>21</td><td>60%</td><td>14</td><td>40%</td><td>20</td><td>61%</td><td>13</td><td>39%</td></tr><tr><td>Unknown</td><td>17</td><td>71%</td><td>7</td><td>29%</td><td>17</td><td>77%</td><td>5</td><td>23%</td></tr><tr><td rowspan="3">Pre-hospital hypotension (SBP &lt; 90)</td><td>No</td><td>96</td><td>58%</td><td>69</td><td>42%</td><td rowspan="3">0.47</td><td>83</td><td>60%</td><td>56</td><td>40%</td></tr><tr><td>Yes</td><td>6</td><td>75%</td><td>2</td><td>25%</td><td>7</td><td>88%</td><td>1</td><td>13%</td></tr><tr><td>Unknown</td><td>25</td><td>66%</td><td>13</td><td>34%</td><td>31</td><td>82%</td><td>7</td><td>18%</td></tr></tbody></table> |                                                                  |                                                                | 3 Months, n = 211 |         |  |  |  | 6 Months, n = 185 |  |  |  | Variable |  | GOSE < 8 (n = 127) |  | GOSE ≥ 8 (n = 84) |  | p-Value | GOSE < 8 (n = 121) |  | GOSE ≥ 8 (n = 64) |  | Age | Years (med, IQR) | 40 | 26–54 | 36 | 26–50 | 0.30 | 40 | 26–52 | 35 | 24–51 | Gender | Male | 84 | 59% | 59 | 41% | 0.55 | 79 | 63% | 46 | 37% | Female | 43 | 63% | 25 | 37% | 42 | 70% | 18 | 30% | Race | Caucasian | 83 | 54% | 72 | 46% | 0.02 | 80 | 60% | 54 | 40% | African American or African | 18 | 75% | 6 | 25% | 15 | 75% | 5 | 25% | Asian | 12 | 86% | 2 | 14% | 12 | 92% | 1 | 8% | American Indian or Alaskan | 2 | 100% | 0 | 0% | 2 | 100% | 0 | 0% | Hawaiian or Pacific Islander | 2 | 100% | 0 | 0% | 4 | 100% | 0 | 0% | More than One Race | 6 | 60% | 4 | 40% | 7 | 64% | 4 | 36% |  | Not Available | 1 | 100% | 0 | 0% |  | 1 | 100% | 0 | 0% | Ethnicity | Non-Hispanic | 96 | 58% | 70 | 42% | 0.23 | 91 | 61% | 57 | 39% | Hispanic | 31 | 69% | 14 | 31% | 30 | 83% | 7 | 19% | Years of Education | Years (med, IQR) | 13 | 12–16 | 15 | 12.5–16 | 0.006 | 14 | 12–16 | 15 | 13–16.5 | Psychiatric History | No | 72 | 53% | 63 | 47% | <0.01 | 63 | 56% | 50 | 44% | Yes | 55 | 72% | 21 | 26% | 58 | 81% | 14 | 19% | Injury Mechanism | Fall/Accident/Other | 101 | 56% | 78 | 44% | 0.01 | 95 | 62% | 59 | 38% | Assault | 26 | 81% | 6 | 19% | 26 | 84% | 5 | 16% | Glasgow Coma Scale | 13 | 5 | 71% | 2 | 29% | 0.81 | 5 | 100% | 0 | 0% | 14 | 28 | 62% | 17 | 38% | 24 | 60% | 16 | 40% | 15 | 94 | 59% | 65 | 41% | 92 | 66% | 48 | 34% | Anticoagulant Use | No | 120 | 60% | 79 | 40% | >0.99 | 112 | 63% | 61 | 35% | Yes | 7 | 58% | 5 | 42% | 9 | 75% | 3 | 25% | Loss of consciousness | None | 39 | 61% | 25 | 39% | 0.58 | 31 | 60% | 21 | 40% | < 30 min | 54 | 37% | 41 | 47% | 59 | 69% | 27 | 31% | ≥ 30 min | 4 | 50% | 4 | 50% | 7 | 64% | 4 | 36% | Unknown | 30 | 68% | 14 | 32% | 24 | 67% | 12 | 33% | Post-traumatic amnesia | None | 48 | 61% | 31 | 39% | 0.66 | 45 | 63% | 26 | 37% | < 30 min | 41 | 56% | 32 | 44% | 39 | 66% | 13 | 34% | ≥ 30 min | 21 | 60% | 14 | 40% | 20 | 61% | 13 | 39% | Unknown | 17 | 71% | 7 | 29% | 17 | 77% | 5 | 23% | Pre-hospital hypotension (SBP < 90) | No | 96 | 58% | 69 | 42% | 0.47 | 83 | 60% | 56 | 40% | Yes | 6 | 75% | 2 | 25% | 7 | 88% | 1 | 13% | Unknown | 25 | 66% | 13 | 34% | 31 | 82% | 7 | 18% | 76% of 275 | 88% at 6 months | 13 |
|                                     |                                                                                                                                                  | 3 Months, n = 211        |       |                   |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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| Variable                            |                                                                                                                                                  | GOSE < 8 (n = 127)       |       | GOSE ≥ 8 (n = 84) |                         | p-Value                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | GOSE < 8 (n = 121)                                               |                                                                | GOSE ≥ 8 (n = 64) |         |  |  |  |                   |  |  |  |          |  |                    |  |                   |  |         |                    |  |                   |  |     |                  |    |       |    |       |      |    |       |    |       |        |      |    |     |    |     |      |    |     |    |     |        |    |     |    |     |    |     |    |     |      |           |    |     |    |     |      |    |     |    |     |                             |    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| Age                                 | Years (med, IQR)                                                                                                                                 | 40                       | 26–54 | 36                | 26–50                   | 0.30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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| Gender                              | Male                                                                                                                                             | 84                       | 59%   | 59                | 41%                     | 0.55                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|                                     | Female                                                                                                                                           | 43                       | 63%   | 25                | 37%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Race                                | Caucasian                                                                                                                                        | 83                       | 54%   | 72                | 46%                     | 0.02                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | African American or African                                                                                                                      | 18                       | 75%   | 6                 | 25%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | Asian                                                                                                                                            | 12                       | 86%   | 2                 | 14%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | American Indian or Alaskan                                                                                                                       | 2                        | 100%  | 0                 | 0%                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | Hawaiian or Pacific Islander                                                                                                                     | 2                        | 100%  | 0                 | 0%                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | More than One Race                                                                                                                               | 6                        | 60%   | 4                 | 40%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | Not Available                                                                                                                                    | 1                        | 100%  | 0                 | 0%                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |    |     |    |     |    |     |                   |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |   |     |   |     |                       |      |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |    |     |          |   |     |   |     |   |     |   |     |         |    |     |    |     |    |     |    |     |                        |      |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |    |     |          |    |     |    |     |    |     |    |     |         |    |     |   |     |    |     |   |     |                                     |    |    |     |    |     |      |    |     |    |     |     |   |     |   |     |   |     |   |     |         |    |     |    |     |    |     |   |     |            |                 |    |
| Ethnicity                           | Non-Hispanic                                                                                                                                     | 96                       | 58%   | 70                | 42%                     | 0.23                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | Hispanic                                                                                                                                         | 31                       | 69%   | 14                | 31%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Years of Education                  | Years (med, IQR)                                                                                                                                 | 13                       | 12–16 | 15                | 12.5–16                 | 0.006                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Psychiatric History                 | No                                                                                                                                               | 72                       | 53%   | 63                | 47%                     | <0.01                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | Yes                                                                                                                                              | 55                       | 72%   | 21                | 26%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |    |     |    |     |    |     |                   |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |   |     |   |     |                       |      |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |    |     |          |   |     |   |     |   |     |   |     |         |    |     |    |     |    |     |    |     |                        |      |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |    |     |          |    |     |    |     |    |     |    |     |         |    |     |   |     |    |     |   |     |                                     |    |    |     |    |     |      |    |     |    |     |     |   |     |   |     |   |     |   |     |         |    |     |    |     |    |     |   |     |            |                 |    |
| Injury Mechanism                    | Fall/Accident/Other                                                                                                                              | 101                      | 56%   | 78                | 44%                     | 0.01                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |    |     |    |     |    |     |                   |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |   |     |   |     |                       |      |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |    |     |          |   |     |   |     |   |     |   |     |         |    |     |    |     |    |     |    |     |                        |      |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |    |     |          |    |     |    |     |    |     |    |     |         |    |     |   |     |    |     |   |     |                                     |    |    |     |    |     |      |    |     |    |     |     |   |     |   |     |   |     |   |     |         |    |     |    |     |    |     |   |     |            |                 |    |
|                                     | Assault                                                                                                                                          | 26                       | 81%   | 6                 | 19%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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| Glasgow Coma Scale                  | 13                                                                                                                                               | 5                        | 71%   | 2                 | 29%                     | 0.81                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | 14                                                                                                                                               | 28                       | 62%   | 17                | 38%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | 15                                                                                                                                               | 94                       | 59%   | 65                | 41%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Anticoagulant Use                   | No                                                                                                                                               | 120                      | 60%   | 79                | 40%                     | >0.99                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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|                                     | Yes                                                                                                                                              | 7                        | 58%   | 5                 | 42%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Loss of consciousness               | None                                                                                                                                             | 39                       | 61%   | 25                | 39%                     | 0.58                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|                                     | < 30 min                                                                                                                                         | 54                       | 37%   | 41                | 47%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | ≥ 30 min                                                                                                                                         | 4                        | 50%   | 4                 | 50%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | Unknown                                                                                                                                          | 30                       | 68%   | 14                | 32%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Post-traumatic amnesia              | None                                                                                                                                             | 48                       | 61%   | 31                | 39%                     | 0.66                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|                                     | < 30 min                                                                                                                                         | 41                       | 56%   | 32                | 44%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | ≥ 30 min                                                                                                                                         | 21                       | 60%   | 14                | 40%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 20                                                               | 61%                                                            | 13                | 39%     |  |  |  |                   |  |  |  |          |  |                    |  |                   |  |         |                    |  |                   |  |     |                  |    |       |    |       |      |    |       |    |       |        |      |    |     |    |     |      |    |     |    |     |        |    |     |    |     |    |     |    |     |      |           |    |     |    |     |      |    |     |    |     |                             |    |     |   |     |    |     |   |     |       |    |     |   |     |    |     |   |    |                            |   |      |   |    |   |      |   |    |                              |   |      |   |    |   |      |   |    |                    |   |     |   |     |   |     |   |     |  |               |   |      |   |    |  |   |      |   |    |           |              |    |     |    |     |      |    |     |    |     |          |    |     |    |     |    |     |   |     |                    |                  |    |       |    |         |       |    |       |    |         |                     |    |    |     |    |     |       |    |     |    |     |     |    |     |    |     |    |     |    |     |                  |                     |     |     |    |     |      |    |     |    |     |         |    |     |   |     |    |     |   |     |                    |    |   |     |   |     |      |   |      |   |    |    |    |     |    |     |    |     |    |     |    |    |     |   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|                                     | Unknown                                                                                                                                          | 17                       | 71%   | 7                 | 29%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Pre-hospital hypotension (SBP < 90) | No                                                                                                                                               | 96                       | 58%   | 69                | 42%                     | 0.47                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|                                     | Yes                                                                                                                                              | 6                        | 75%   | 2                 | 25%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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|                                     | Unknown                                                                                                                                          | 25                       | 66%   | 13                | 34%                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| Reference                                       | Population                                                                                                                                                                                                                                                                 | Study Design                                      |      | Outcomes             | Time points and factors                    | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up             | Quality appraisal |     |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|------|----------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------------|-------------------|-----|--|--|-------------------|--|--|--|--|--|----------|--|-----------------------|--|----------------------|---------|-----------------------|--|-----------------------|--|-------------------------------------------------|----|----|-----|----|-----|------|----|-----|----|-----|-----|---|------|---|----|--|---|------|---|----|---------|----|-----|----|-----|--|----|-----|---|-----|-------------------------|----------|-----|-----|----|-----|------|-----|-----|----|-----|----------|---|-----|---|-----|--|---|-----|---|-----|---------------------|----------|----|-----|----|-----|------|----|-----|----|-----|----------|----|-----|---|-----|--|----|-----|---|-----|--------------|----|-----|----|-----|--|----|-----|----|-----|----------------|----|-----|-----|----|-----|-------|-----|-----|----|-----|-----|---|-----|---|-----|--|---|------|---|----|---------|---|------|---|----|--|---|----|---|----|------------|----|-----|-----|----|-----|-------|-----|-----|----|-----|-----|---|-----|---|-----|--|---|-----|---|-----|---------|---|------|---|----|--|---|------|---|----|--|--|--|
|                                                 |                                                                                                                                                                                                                                                                            |                                                   |      |                      |                                            | <table><tr><th colspan="6">3 Months, n = 211</th><th colspan="6">6 Months, n = 185</th></tr><tr><th>Variable</th><th></th><th>GOSE &lt; 8<br/>(n = 127)</th><th></th><th>GOSE ≥ 8<br/>(n = 84)</th><th>p-Value</th><th>GOSE &lt; 8<br/>(n = 122)</th><th></th><th>GOSE ≥ 8<br/>(n = 148)</th><th></th></tr><tr><td rowspan="3">Pre-hospital hypoxia<br/>(SpO<sub>2</sub> &lt; 90)</td><td>No</td><td>96</td><td>38%</td><td>70</td><td>42%</td><td>0.08</td><td>85</td><td>60%</td><td>56</td><td>40%</td></tr><tr><td>Yes</td><td>5</td><td>100%</td><td>0</td><td>0%</td><td></td><td>3</td><td>100%</td><td>0</td><td>0%</td></tr><tr><td>Unknown</td><td>26</td><td>65%</td><td>14</td><td>35%</td><td></td><td>33</td><td>80%</td><td>8</td><td>20%</td></tr><tr><td rowspan="2">Urine toxicology screen</td><td>Negative</td><td>120</td><td>61%</td><td>78</td><td>39%</td><td>0.77</td><td>113</td><td>65%</td><td>62</td><td>35%</td></tr><tr><td>Positive</td><td>7</td><td>54%</td><td>6</td><td>46%</td><td></td><td>8</td><td>80%</td><td>2</td><td>20%</td></tr><tr><td rowspan="3">Blood alcohol level</td><td>Negative</td><td>27</td><td>60%</td><td>18</td><td>40%</td><td>0.66</td><td>23</td><td>62%</td><td>14</td><td>38%</td></tr><tr><td>Positive</td><td>16</td><td>70%</td><td>7</td><td>30%</td><td></td><td>18</td><td>78%</td><td>5</td><td>22%</td></tr><tr><td>Not obtained</td><td>84</td><td>59%</td><td>59</td><td>41%</td><td></td><td>80</td><td>64%</td><td>45</td><td>36%</td></tr><tr><td rowspan="3">ED hypotension</td><td>No</td><td>125</td><td>60%</td><td>83</td><td>40%</td><td>&gt;0.99</td><td>119</td><td>65%</td><td>64</td><td>35%</td></tr><tr><td>Yes</td><td>1</td><td>50%</td><td>1</td><td>50%</td><td></td><td>2</td><td>100%</td><td>0</td><td>0%</td></tr><tr><td>Unknown</td><td>1</td><td>100%</td><td>0</td><td>0%</td><td></td><td>0</td><td>0%</td><td>0</td><td>0%</td></tr><tr><td rowspan="3">ED hypoxia</td><td>No</td><td>120</td><td>60%</td><td>81</td><td>40%</td><td>&gt;0.99</td><td>116</td><td>65%</td><td>62</td><td>35%</td></tr><tr><td>Yes</td><td>5</td><td>63%</td><td>3</td><td>38%</td><td></td><td>4</td><td>67%</td><td>2</td><td>33%</td></tr><tr><td>Unknown</td><td>2</td><td>100%</td><td>0</td><td>0%</td><td></td><td>1</td><td>100%</td><td>0</td><td>0%</td></tr></table> <p>Caption: ED—emergency department; IQR—interquartile range; GOSE—Glasgow Outcome Scale—Extended; SBP—systolic blood pressure; SpO<sub>2</sub>—oxygen saturation measurement. Bold font designates <i>p</i> &lt; 0.05.</p> | 3 Months, n = 211                                                |                                                                            |                   |     |  |  | 6 Months, n = 185 |  |  |  |  |  | Variable |  | GOSE < 8<br>(n = 127) |  | GOSE ≥ 8<br>(n = 84) | p-Value | GOSE < 8<br>(n = 122) |  | GOSE ≥ 8<br>(n = 148) |  | Pre-hospital hypoxia<br>(SpO <sub>2</sub> < 90) | No | 96 | 38% | 70 | 42% | 0.08 | 85 | 60% | 56 | 40% | Yes | 5 | 100% | 0 | 0% |  | 3 | 100% | 0 | 0% | Unknown | 26 | 65% | 14 | 35% |  | 33 | 80% | 8 | 20% | Urine toxicology screen | Negative | 120 | 61% | 78 | 39% | 0.77 | 113 | 65% | 62 | 35% | Positive | 7 | 54% | 6 | 46% |  | 8 | 80% | 2 | 20% | Blood alcohol level | Negative | 27 | 60% | 18 | 40% | 0.66 | 23 | 62% | 14 | 38% | Positive | 16 | 70% | 7 | 30% |  | 18 | 78% | 5 | 22% | Not obtained | 84 | 59% | 59 | 41% |  | 80 | 64% | 45 | 36% | ED hypotension | No | 125 | 60% | 83 | 40% | >0.99 | 119 | 65% | 64 | 35% | Yes | 1 | 50% | 1 | 50% |  | 2 | 100% | 0 | 0% | Unknown | 1 | 100% | 0 | 0% |  | 0 | 0% | 0 | 0% | ED hypoxia | No | 120 | 60% | 81 | 40% | >0.99 | 116 | 65% | 62 | 35% | Yes | 5 | 63% | 3 | 38% |  | 4 | 67% | 2 | 33% | Unknown | 2 | 100% | 0 | 0% |  | 1 | 100% | 0 | 0% |  |  |  |
| 3 Months, n = 211                               |                                                                                                                                                                                                                                                                            |                                                   |      |                      |                                            | 6 Months, n = 185                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                            |                   |     |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| Variable                                        |                                                                                                                                                                                                                                                                            | GOSE < 8<br>(n = 127)                             |      | GOSE ≥ 8<br>(n = 84) | p-Value                                    | GOSE < 8<br>(n = 122)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                  | GOSE ≥ 8<br>(n = 148)                                                      |                   |     |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| Pre-hospital hypoxia<br>(SpO <sub>2</sub> < 90) | No                                                                                                                                                                                                                                                                         | 96                                                | 38%  | 70                   | 42%                                        | 0.08                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 85                                                               | 60%                                                                        | 56                | 40% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Yes                                                                                                                                                                                                                                                                        | 5                                                 | 100% | 0                    | 0%                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 3                                                                | 100%                                                                       | 0                 | 0%  |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Unknown                                                                                                                                                                                                                                                                    | 26                                                | 65%  | 14                   | 35%                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 33                                                               | 80%                                                                        | 8                 | 20% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| Urine toxicology screen                         | Negative                                                                                                                                                                                                                                                                   | 120                                               | 61%  | 78                   | 39%                                        | 0.77                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 113                                                              | 65%                                                                        | 62                | 35% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Positive                                                                                                                                                                                                                                                                   | 7                                                 | 54%  | 6                    | 46%                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 8                                                                | 80%                                                                        | 2                 | 20% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| Blood alcohol level                             | Negative                                                                                                                                                                                                                                                                   | 27                                                | 60%  | 18                   | 40%                                        | 0.66                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 23                                                               | 62%                                                                        | 14                | 38% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Positive                                                                                                                                                                                                                                                                   | 16                                                | 70%  | 7                    | 30%                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 18                                                               | 78%                                                                        | 5                 | 22% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Not obtained                                                                                                                                                                                                                                                               | 84                                                | 59%  | 59                   | 41%                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 80                                                               | 64%                                                                        | 45                | 36% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| ED hypotension                                  | No                                                                                                                                                                                                                                                                         | 125                                               | 60%  | 83                   | 40%                                        | >0.99                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 119                                                              | 65%                                                                        | 64                | 35% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Yes                                                                                                                                                                                                                                                                        | 1                                                 | 50%  | 1                    | 50%                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 2                                                                | 100%                                                                       | 0                 | 0%  |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Unknown                                                                                                                                                                                                                                                                    | 1                                                 | 100% | 0                    | 0%                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0                                                                | 0%                                                                         | 0                 | 0%  |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| ED hypoxia                                      | No                                                                                                                                                                                                                                                                         | 120                                               | 60%  | 81                   | 40%                                        | >0.99                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 116                                                              | 65%                                                                        | 62                | 35% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Yes                                                                                                                                                                                                                                                                        | 5                                                 | 63%  | 3                    | 38%                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 4                                                                | 67%                                                                        | 2                 | 33% |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
|                                                 | Unknown                                                                                                                                                                                                                                                                    | 2                                                 | 100% | 0                    | 0%                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1                                                                | 100%                                                                       | 0                 | 0%  |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |
| 11 <sup>11</sup>                                | 18 level 1 trauma centres in the US February 26, 2014, and August 8, 2018. Patients presented within 24 hours of injury and underwent CT imaging.<br><br>Study included participants 17 years and older with moderate TBI (GCS scores 9-12) or severe TBI (GCS scores 3-8) | Prospective multicentre longitudinal cohort study |      | GOSE                 | 2 Weeks and 3, 6, and 12 Months Postinjury |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 69% of 122                                                       | 90% at 6 months<br><br>86% at 12 months<br><br>Some post discharge deaths, | 15                |     |  |  |                   |  |  |  |  |  |          |  |                       |  |                      |         |                       |  |                       |  |                                                 |    |    |     |    |     |      |    |     |    |     |     |   |      |   |    |  |   |      |   |    |         |    |     |    |     |  |    |     |   |     |                         |          |     |     |    |     |      |     |     |    |     |          |   |     |   |     |  |   |     |   |     |                     |          |    |     |    |     |      |    |     |    |     |          |    |     |   |     |  |    |     |   |     |              |    |     |    |     |  |    |     |    |     |                |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |      |   |    |         |   |      |   |    |  |   |    |   |    |            |    |     |     |    |     |       |     |     |    |     |     |   |     |   |     |  |   |     |   |     |         |   |      |   |    |  |   |      |   |    |  |  |  |

| Reference                                      | Population           | Study Design      | Outcomes         | Time points and factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |      |  |      |  |       |  |                  |                   |                  |                   |                  |                   |                  |                   |                                   |  |  |  |  |  |  |  |  |                  |           |         |          |   |         |   |         |   |      |           |       |           |        |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |           |         |           |         |           |    |                  |         |       |           |         |           |         |          |   |                           |            |         |            |         |           |         |           |    |                                       |  |  |  |  |  |  |  |  |            |          |         |           |         |           |         |           |    |            |         |       |          |         |          |       |           |   |           |          |         |           |         |           |         |           |    |        |            |         |           |         |           |         |           |   |                                                |  |  |  |  |  |  |  |  |               |            |         |            |         |            |         |            |    |            |         |       |          |       |          |       |          |   |          |          |         |           |         |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
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|                                                |                      |                   |                  |                         | <p>Table 2. Frequencies Within Each Glasgow Outcome Scale-Extended (GOSE) Domain for Severe and Moderate Traumatic Brain Injury (TBI) Groups at 2 Weeks and 3, 6, and 12 Months Postinjury</p> <table> <tr> <th rowspan="2"></th><th colspan="2">No. (%)<sup>a</sup></th><th colspan="2">3 mo</th><th colspan="2">6 mo</th><th colspan="2">12 mo</th></tr> <tr> <th>Severe (n = 290)</th><th>Moderate (n = 93)</th><th>Severe (n = 278)</th><th>Moderate (n = 84)</th><th>Severe (n = 282)</th><th>Moderate (n = 75)</th><th>Severe (n = 271)</th><th>Moderate (n = 75)</th></tr> <tr> <td colspan="9"><b>Vegetative state and death</b></td></tr> <tr> <td>Vegetative state</td><td>68 (23.4)</td><td>11 (12)</td><td>10 (3.6)</td><td>0</td><td>4 (1.4)</td><td>0</td><td>1 (0.4)</td><td>0</td></tr> <tr> <td>Died</td><td>60 (20.7)</td><td>4 (4)</td><td>73 (26.3)</td><td>9 (11)</td><td>78 (27.7)</td><td>9 (12)</td><td>83 (30.6)</td><td>9</td></tr> <tr> <td colspan="9"><b>Independence in the home</b></td></tr> <tr> <td>No assistance</td><td>31 (10.7)</td><td>36 (39)</td><td>115 (41.4)</td><td>55 (65)</td><td>139 (49.3)</td><td>51 (68)</td><td>137 (50.6)</td><td>54</td></tr> <tr> <td>Infrequent assistance</td><td>5 (1.7)</td><td>2 (2)</td><td>9 (3.2)</td><td>3 (4)</td><td>6 (2.1)</td><td>2 (3)</td><td>5 (1.8)</td><td>4</td></tr> <tr> <td>Frequent assistance</td><td>126 (43.4)</td><td>40 (43)</td><td>71 (25.5)</td><td>17 (20)</td><td>55 (19.5)</td><td>13 (17)</td><td>45 (16.6)</td><td>9</td></tr> <tr> <td colspan="9"><b>Independence in shopping</b></td></tr> <tr> <td>No assistance</td><td>33 (11.4)</td><td>36 (39)</td><td>115 (41.4)</td><td>54 (64)</td><td>140 (49.6)</td><td>48 (64)</td><td>135 (49.8)</td><td>42</td></tr> <tr> <td>Assistance</td><td>128 (44.3)</td><td>42 (45)</td><td>80 (28.8)</td><td>21 (25)</td><td>60 (21.3)</td><td>18 (24)</td><td>52 (19.2)</td><td>14</td></tr> <tr> <td colspan="9"><b>Independence in traveling</b></td></tr> <tr> <td>No assistance</td><td>33 (11.4)</td><td>34 (37)</td><td>110 (39.6)</td><td>54 (64)</td><td>139 (49.3)</td><td>47 (63)</td><td>133 (49.1)</td><td>46</td></tr> <tr> <td>Assistance</td><td>128 (44.1)</td><td>44 (47)</td><td>85 (30.6)</td><td>21 (25)</td><td>61 (21.6)</td><td>19 (25)</td><td>54 (19.9)</td><td>17</td></tr> <tr> <td colspan="9"><b>Work<sup>b</sup></b></td></tr> <tr> <td>No deficit</td><td>2 (1.0)</td><td>8 (10)</td><td>25 (11.8)</td><td>21 (29)</td><td>57 (26.9)</td><td>23 (37)</td><td>70 (34.0)</td><td>36</td></tr> <tr> <td>Reduced capacity</td><td>3 (1.4)</td><td>4 (5)</td><td>25 (11.8)</td><td>12 (17)</td><td>26 (12.3)</td><td>12 (19)</td><td>20 (9.7)</td><td>7</td></tr> <tr> <td>Limited or unable to work</td><td>133 (63.3)</td><td>55 (70)</td><td>125 (59.2)</td><td>34 (47)</td><td>94 (44.3)</td><td>22 (35)</td><td>79 (38.3)</td><td>15</td></tr> <tr> <td colspan="9"><b>Social and leisure functioning</b></td></tr> <tr> <td>No deficit</td><td>11 (3.8)</td><td>16 (17)</td><td>56 (20.1)</td><td>34 (40)</td><td>92 (32.6)</td><td>34 (45)</td><td>98 (36.2)</td><td>34</td></tr> <tr> <td>A bit less</td><td>9 (3.1)</td><td>7 (8)</td><td>23 (8.3)</td><td>10 (12)</td><td>24 (8.5)</td><td>6 (8)</td><td>28 (10.3)</td><td>9</td></tr> <tr> <td>Much less</td><td>17 (5.9)</td><td>11 (12)</td><td>51 (18.3)</td><td>15 (18)</td><td>38 (13.5)</td><td>15 (20)</td><td>27 (10.0)</td><td>11</td></tr> <tr> <td>Unable</td><td>124 (42.9)</td><td>43 (47)</td><td>65 (23.4)</td><td>16 (19)</td><td>46 (16.3)</td><td>11 (15)</td><td>34 (12.5)</td><td>7</td></tr> <tr> <td colspan="9"><b>Psychological or interpersonal problems</b></td></tr> <tr> <td>No disruption</td><td>101 (34.9)</td><td>38 (41)</td><td>122 (43.9)</td><td>47 (56)</td><td>114 (40.4)</td><td>34 (45)</td><td>109 (40.2)</td><td>35</td></tr> <tr> <td>Occasional</td><td>6 (2.1)</td><td>4 (4)</td><td>16 (5.8)</td><td>5 (6)</td><td>25 (8.9)</td><td>6 (8)</td><td>13 (4.8)</td><td>7</td></tr> <tr> <td>Frequent</td><td>16 (5.5)</td><td>14 (15)</td><td>37 (13.3)</td><td>13 (15)</td><td>40 (14.2)</td><td>18 (24)</td><td>43 (15.9)</td><td>15</td></tr> <tr> <td>Constant</td><td>38 (13.1)</td><td>21 (23)</td><td>20 (7.2)</td><td>10 (12)</td><td>21 (7.4)</td><td>8 (11)</td><td>22 (8.1)</td><td>6</td></tr> <tr> <td colspan="9"><b>Other disabling symptoms</b></td></tr> <tr> <td>No impact</td><td>38 (13.1)</td><td>12 (13)</td><td>49 (17.6)</td><td>14 (17)</td><td>52 (18.4)</td><td>15 (20)</td><td>53 (19.6)</td><td>18</td></tr> <tr> <td>Some impact</td><td>123 (42.6)</td><td>66 (71)</td><td>146 (52.5)</td><td>60 (72)</td><td>148 (52.5)</td><td>51 (68)</td><td>134 (49.4)</td><td>45</td></tr> </table> <p><sup>a</sup> Percentages within each domain sum to 100% after adding percentages of individuals in vegetative state and death categories for the group at each time, with the exception of the work domain, which excludes those who did not work preinjury.</p> <p><sup>b</sup> Work among those who worked preinjury; denominators for these calculations were 210 for those with severe injury at 2 weeks, 79 for those with injury at 2 weeks, 211 for those with severe injury at 3 months, 72 for those with moderate injury at 3 months, 212 for those with severe injury months, 62 for those with moderate injury at 6 months, 206 for those with severe injury at 1 year, and 7 for those with moderate injury at 1 year.</p> |                                                                  | No. (%) <sup>a</sup>                                           |                   | 3 mo |  | 6 mo |  | 12 mo |  | Severe (n = 290) | Moderate (n = 93) | Severe (n = 278) | Moderate (n = 84) | Severe (n = 282) | Moderate (n = 75) | Severe (n = 271) | Moderate (n = 75) | <b>Vegetative state and death</b> |  |  |  |  |  |  |  |  | Vegetative state | 68 (23.4) | 11 (12) | 10 (3.6) | 0 | 4 (1.4) | 0 | 1 (0.4) | 0 | Died | 60 (20.7) | 4 (4) | 73 (26.3) | 9 (11) | 78 (27.7) | 9 (12) | 83 (30.6) | 9 | <b>Independence in the home</b> |  |  |  |  |  |  |  |  | No assistance | 31 (10.7) | 36 (39) | 115 (41.4) | 55 (65) | 139 (49.3) | 51 (68) | 137 (50.6) | 54 | Infrequent assistance | 5 (1.7) | 2 (2) | 9 (3.2) | 3 (4) | 6 (2.1) | 2 (3) | 5 (1.8) | 4 | Frequent assistance | 126 (43.4) | 40 (43) | 71 (25.5) | 17 (20) | 55 (19.5) | 13 (17) | 45 (16.6) | 9 | <b>Independence in shopping</b> |  |  |  |  |  |  |  |  | No assistance | 33 (11.4) | 36 (39) | 115 (41.4) | 54 (64) | 140 (49.6) | 48 (64) | 135 (49.8) | 42 | Assistance | 128 (44.3) | 42 (45) | 80 (28.8) | 21 (25) | 60 (21.3) | 18 (24) | 52 (19.2) | 14 | <b>Independence in traveling</b> |  |  |  |  |  |  |  |  | No assistance | 33 (11.4) | 34 (37) | 110 (39.6) | 54 (64) | 139 (49.3) | 47 (63) | 133 (49.1) | 46 | Assistance | 128 (44.1) | 44 (47) | 85 (30.6) | 21 (25) | 61 (21.6) | 19 (25) | 54 (19.9) | 17 | <b>Work<sup>b</sup></b> |  |  |  |  |  |  |  |  | No deficit | 2 (1.0) | 8 (10) | 25 (11.8) | 21 (29) | 57 (26.9) | 23 (37) | 70 (34.0) | 36 | Reduced capacity | 3 (1.4) | 4 (5) | 25 (11.8) | 12 (17) | 26 (12.3) | 12 (19) | 20 (9.7) | 7 | Limited or unable to work | 133 (63.3) | 55 (70) | 125 (59.2) | 34 (47) | 94 (44.3) | 22 (35) | 79 (38.3) | 15 | <b>Social and leisure functioning</b> |  |  |  |  |  |  |  |  | No deficit | 11 (3.8) | 16 (17) | 56 (20.1) | 34 (40) | 92 (32.6) | 34 (45) | 98 (36.2) | 34 | A bit less | 9 (3.1) | 7 (8) | 23 (8.3) | 10 (12) | 24 (8.5) | 6 (8) | 28 (10.3) | 9 | Much less | 17 (5.9) | 11 (12) | 51 (18.3) | 15 (18) | 38 (13.5) | 15 (20) | 27 (10.0) | 11 | Unable | 124 (42.9) | 43 (47) | 65 (23.4) | 16 (19) | 46 (16.3) | 11 (15) | 34 (12.5) | 7 | <b>Psychological or interpersonal problems</b> |  |  |  |  |  |  |  |  | No disruption | 101 (34.9) | 38 (41) | 122 (43.9) | 47 (56) | 114 (40.4) | 34 (45) | 109 (40.2) | 35 | Occasional | 6 (2.1) | 4 (4) | 16 (5.8) | 5 (6) | 25 (8.9) | 6 (8) | 13 (4.8) | 7 | Frequent | 16 (5.5) | 14 (15) | 37 (13.3) | 13 (15) | 40 (14.2) | 18 (24) | 43 (15.9) | 15 | Constant | 38 (13.1) | 21 (23) | 20 (7.2) | 10 (12) | 21 (7.4) | 8 (11) | 22 (8.1) | 6 | <b>Other disabling symptoms</b> |  |  |  |  |  |  |  |  | No impact | 38 (13.1) | 12 (13) | 49 (17.6) | 14 (17) | 52 (18.4) | 15 (20) | 53 (19.6) | 18 | Some impact | 123 (42.6) | 66 (71) | 146 (52.5) | 60 (72) | 148 (52.5) | 51 (68) | 134 (49.4) | 45 |  |  |  |
|                                                | No. (%) <sup>a</sup> |                   | 3 mo             |                         | 6 mo                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |        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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
|                                                | Severe (n = 290)     | Moderate (n = 93) | Severe (n = 278) | Moderate (n = 84)       | Severe (n = 282)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Moderate (n = 75)                                                | Severe (n = 271)                                               | Moderate (n = 75) |      |  |      |  |       |  |                  |                   |                  |                   |                  |                   |                  |                   |                                   |  |  |  |  |  |  |  |  |                  |           |         |          |   |         |   |         |   |      |           |       |           |        |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |           |         |           |         |           |    |                  |         |       |           |         |           |         |          |   |                           |            |         |            |         |           |         |           |    |                                       |  |  |  |  |  |  |  |  |            |          |         |           |         |           |         |           |    |            |         |       |          |         |          |       |           |   |           |          |         |           |         |           |         |           |    |        |            |         |           |         |           |         |           |   |                                                |  |  |  |  |  |  |  |  |               |            |         |            |         |            |         |            |    |            |         |       |          |       |          |       |          |   |          |          |         |           |         |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| <b>Vegetative state and death</b>              |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |        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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| Vegetative state                               | 68 (23.4)            | 11 (12)           | 10 (3.6)         | 0                       | 4 (1.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0                                                                | 1 (0.4)                                                        | 0                 |      |  |      |  |       |  |                  |                   |                  |                   |                  |                   |                  |                   |                                   |  |  |  |  |  |  |  |  |                  |           |         |          |   |         |   |         |   |      |           |       |           |        |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |        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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| Died                                           | 60 (20.7)            | 4 (4)             | 73 (26.3)        | 9 (11)                  | 78 (27.7)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 9 (12)                                                           | 83 (30.6)                                                      | 9                 |      |  |      |  |       |  |                  |                   |                  |                   |                  |                   |                  |                   |                                   |  |  |  |  |  |  |  |  |                  |           |         |          |   |         |   |         |   |      |           |       |           |        |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |        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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| <b>Independence in the home</b>                |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| No assistance                                  | 31 (10.7)            | 36 (39)           | 115 (41.4)       | 55 (65)                 | 139 (49.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Infrequent assistance                          | 5 (1.7)              | 2 (2)             | 9 (3.2)          | 3 (4)                   | 6 (2.1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| Frequent assistance                            | 126 (43.4)           | 40 (43)           | 71 (25.5)        | 17 (20)                 | 55 (19.5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| <b>Independence in shopping</b>                |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| No assistance                                  | 33 (11.4)            | 36 (39)           | 115 (41.4)       | 54 (64)                 | 140 (49.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |        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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| Assistance                                     | 128 (44.3)           | 42 (45)           | 80 (28.8)        | 21 (25)                 | 60 (21.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| <b>Independence in traveling</b>               |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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   |         |           |         |           |    |                  |         |       |           |         |           |         |          |   |                           |            |         |            |         |           |         |           |    |                                       |  |  |  |  |  |  |  |  |            |          |         |           |         |           |         |           |    |            |         |       |          |         |          |       |           |   |           |          |         |           |         |           |         |           |    |        |            |         |           |         |           |         |           |   |                                                |  |  |  |  |  |  |  |  |               |            |         |            |         |            |         |            |    |            |         |       |          |       |          |       |          |   |          |          |         |           |         |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| No assistance                                  | 33 (11.4)            | 34 (37)           | 110 (39.6)       | 54 (64)                 | 139 (49.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Assistance                                     | 128 (44.1)           | 44 (47)           | 85 (30.6)        | 21 (25)                 | 61 (21.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |           |         |           |         |           |    |                  |         |       |           |         |           |         |          |   |                           |            |         |            |         |           |         |           |    |                                       |  |  |  |  |  |  |  |  |            |          |         |           |         |           |         |           |    |            |         |       |          |         |          |       |           |   |           |          |         |           |         |           |         |           |    |        |            |         |           |         |           |         |           |   |                                                |  |  |  |  |  |  |  |  |               |            |         |            |         |            |         |            |    |            |         |       |          |       |          |       |          |   |          |          |         |           |   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| <b>Work<sup>b</sup></b>                        |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| No deficit                                     | 2 (1.0)              | 8 (10)            | 25 (11.8)        | 21 (29)                 | 57 (26.9)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| Reduced capacity                               | 3 (1.4)              | 4 (5)             | 25 (11.8)        | 12 (17)                 | 26 (12.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| Limited or unable to work                      | 133 (63.3)           | 55 (70)           | 125 (59.2)       | 34 (47)                 | 94 (44.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| <b>Social and leisure functioning</b>          |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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      |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| No deficit                                     | 11 (3.8)             | 16 (17)           | 56 (20.1)        | 34 (40)                 | 92 (32.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |        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| A bit less                                     | 9 (3.1)              | 7 (8)             | 23 (8.3)         | 10 (12)                 | 24 (8.5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |           |         |           |         |           |    |                  |         |       |           |         |           |         |          |   |                           |            |         |            |         |           |         |           |    |                                       |  |  |  |  |  |  |  |  |            |          |         |           |         |           |         |           |    |            |         |       |          |         |          |       |           |   |           |          |         |           |         |           |         |           |    |        |            |         |           |         |           |         |           |   |                                                |  |  |  |  |  |  |  |  |               |            |         |            |         |            |         |            |    |            |         |       |          |       |          |       |          |   |          |          |         |           |         |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| Much less                                      | 17 (5.9)             | 11 (12)           | 51 (18.3)        | 15 (18)                 | 38 (13.5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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 |           |        |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |                       |         |       |         |       |         |       |         |   |                     |            |         |           |         |           |         |           |   |                                 |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                                  |  |  |  |  |  |  |  |  |               |           |         |            |         |            |         |            |    |            |            |         |           |         |           |         |           |    |                         |  |  |  |  |  |  |  |  |            |         |        |           |         |           |         |           |    |                  |         |       |           |         |           |         |          |   |                           |            |         |            |         |           |         |           |    |                                       |  |  |  |  |  |  |  |  |            |          |         |           |         |           |         |           |    |            |         |       |          |         |          |       |           |   |           |          |         |           |         |           |         |           |    |        |            |         |           |         |           |         |           |   |                                                |  |  |  |  |  |  |  |  |               |            |         |            |         |            |         |            |    |            |         |       |          |       |          |       |          |   |          |          |         |           |         |           |         |           |    |          |           |         |          |         |          |        |          |   |                                 |  |  |  |  |  |  |  |  |           |           |         |           |         |           |         |           |    |             |            |         |            |         |            |         |            |    |  |  |  |
| Unable                                         | 124 (42.9)           | 43 (47)           | 65 (23.4)        | 16 (19)                 | 46 (16.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| <b>Psychological or interpersonal problems</b> |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| No disruption                                  | 101 (34.9)           | 38 (41)           | 122 (43.9)       | 47 (56)                 | 114 (40.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Occasional                                     | 6 (2.1)              | 4 (4)             | 16 (5.8)         | 5 (6)                   | 25 (8.9)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| Frequent                                       | 16 (5.5)             | 14 (15)           | 37 (13.3)        | 13 (15)                 | 40 (14.2)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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| Constant                                       | 38 (13.1)            | 21 (23)           | 20 (7.2)         | 10 (12)                 | 21 (7.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| <b>Other disabling symptoms</b>                |                      |                   |                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| No impact                                      | 38 (13.1)            | 12 (13)           | 49 (17.6)        | 14 (17)                 | 52 (18.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 15 (20)                                                          | 53 (19.6)                                                      | 18                |      |  |      |  |       |  |                  |                   |                  |                   |                  |                   |                  |                   |                                   |  |  |  |  |  |  |  |  |                  |           |         |          |   |         |   |         |   |      |           |       |           |       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| Some impact                                    | 123 (42.6)           | 66 (71)           | 146 (52.5)       | 60 (72)                 | 148 (52.5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Reference           | Population                                                                                                                                                   | Study Design                                      |                  | Outcomes                                                                                                                                                                         | Time points and factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|------------------|--|-------------------|--------------------|-----------|---------------|-----------|---------------|-----------|--------------------|-----------|------|------------|------|-----------|-------------------|-----------|------|------------|------|-----------|--------------------|-----------|------|------------|------|-----------|--------------------|-----------|------|------------|------|-----------|----------------|-----------|------|------------|------|-----------|------------------|-----------|-----------------------------------|------------------|-----------|------|------------------|-----------|------|-------------------|-----------|------|--------------------|-------------|------|---------------------|-------------|------|------------------|------------|------|-------------------|------------|------|--------------------|-------------|-----|---------------------|-------------|-----|------------|-----------------------------------------------------------------------------------|----|
| 12 <sup>12</sup>    | Three level 1 trauma centres. Patients had to present within 24 h of injury undergo CT imaging. Patient included were aged 18 and over, admission GCS 13–15. | Prospective multicentre longitudinal cohort study |                  | Postconcussion syndrome symptoms assessed using a symptom checklist, containing 22 subjective questions classified into four domains: physical; cognitive; emotional; and sleep. | 3, 6, and 12 months     | <div>TABLE 2. MEAN SYMPTOMS REPORTED AND PERCENTAGE REPORTING MORE THAN ONE SYMPTOM FOR ALL FOLLOW-UP TIME, BY TOTAL PCS SYMPTOMS AND EACH PCS FUNCTIONAL DOMAIN</div> <table><tr><th></th><th colspan="2">3 months (N=348)</th><th colspan="2">6 months (N=305)</th><th>12 months (N=285)</th></tr><tr><th>PCS symptom domain</th><th>Mean (SD)</th><th>% ≥ 1 symptom</th><th>Mean (SD)</th><th>% ≥ 1 symptom</th><th>Mean (SD)</th></tr><tr><td>Total PCS symptoms</td><td>5.8 (5.8)</td><td>74.7</td><td>7.3 (6.1)*</td><td>82.4</td><td>6.8 (6.0)</td></tr><tr><td>Physical symptoms</td><td>2.4 (2.6)</td><td>67.0</td><td>2.9 (2.8)*</td><td>71.8</td><td>2.8 (2.8)</td></tr><tr><td>Cognitive symptoms</td><td>1.4 (1.6)</td><td>49.4</td><td>1.7 (1.7)*</td><td>59.3</td><td>1.7 (1.7)</td></tr><tr><td>Emotional symptoms</td><td>1.1 (1.5)</td><td>43.4</td><td>1.5 (1.5)*</td><td>56.7</td><td>1.3 (1.5)</td></tr><tr><td>Sleep symptoms</td><td>1.0 (1.1)</td><td>50.2</td><td>1.3 (1.2)*</td><td>60.3</td><td>1.1 (1.2)</td></tr></table> <div>*p&lt;0.05, compared to immediately previous follow-up time; †p&lt;0.05, compared to 3-month follow-up time. PCS, postconcussion syndrome; SD, standard deviation.</div> <div>TABLE 3. MEAN SCORE AND PERCENT OF PATIENTS WITH CLINICALLY SIGNIFICANT IMPAIRMENT, DISTRESS OR DISSATISFACTION FOR THE GOSE, BSI, SWLS, AND RPQ-13, RESPECTIVELY, (AND WHERE APPLICABLE) AT EACH FOLLOW-UP TIME POINT</div> <table><tr><th>Outcome and time</th><th>Mean (SD)</th><th>% with clinically poorer outcomes</th></tr><tr><td>GOSE at 3 months</td><td>6.9 (1.1)</td><td>33.2</td></tr><tr><td>GOSE at 6 months</td><td>6.9 (1.0)</td><td>33.8</td></tr><tr><td>GOSE at 12 months</td><td>7.1 (1.0)</td><td>22.4</td></tr><tr><td>BSI-18 at 6 months</td><td>55.6 (10.7)</td><td>29.6</td></tr><tr><td>BSI-18 at 12 months</td><td>51.8 (11.1)</td><td>21.1</td></tr><tr><td>SWLS at 6 months</td><td>20.3 (8.0)</td><td>44.5</td></tr><tr><td>SWLS at 12 months</td><td>22.0 (8.2)</td><td>40.3</td></tr><tr><td>RPQ-13 at 6 months</td><td>14.6 (12.2)</td><td>n/a</td></tr><tr><td>RPQ-13 at 12 months</td><td>11.7 (11.3)</td><td>n/a</td></tr></table> <div>Mean (SD) scores reflect only those patients with data available for all applicable follow-up times. Percent scores include the total number of patients at each follow-up time.</div> <div>GOSE, Glasgow Outcome Scale-Extended; BSI, Brief Symptom Inventory; SWLS, Satisfaction With Life Scale; RPQ, Rivermead Post-Concussion Questionnaire; SD, standard deviation; n/a, not available.</div> |                                                                  | 3 months (N=348)                                               |                   | 6 months (N=305) |  | 12 months (N=285) | PCS symptom domain | Mean (SD) | % ≥ 1 symptom | Mean (SD) | % ≥ 1 symptom | Mean (SD) | Total PCS symptoms | 5.8 (5.8) | 74.7 | 7.3 (6.1)* | 82.4 | 6.8 (6.0) | Physical symptoms | 2.4 (2.6) | 67.0 | 2.9 (2.8)* | 71.8 | 2.8 (2.8) | Cognitive symptoms | 1.4 (1.6) | 49.4 | 1.7 (1.7)* | 59.3 | 1.7 (1.7) | Emotional symptoms | 1.1 (1.5) | 43.4 | 1.5 (1.5)* | 56.7 | 1.3 (1.5) | Sleep symptoms | 1.0 (1.1) | 50.2 | 1.3 (1.2)* | 60.3 | 1.1 (1.2) | Outcome and time | Mean (SD) | % with clinically poorer outcomes | GOSE at 3 months | 6.9 (1.1) | 33.2 | GOSE at 6 months | 6.9 (1.0) | 33.8 | GOSE at 12 months | 7.1 (1.0) | 22.4 | BSI-18 at 6 months | 55.6 (10.7) | 29.6 | BSI-18 at 12 months | 51.8 (11.1) | 21.1 | SWLS at 6 months | 20.3 (8.0) | 44.5 | SWLS at 12 months | 22.0 (8.2) | 40.3 | RPQ-13 at 6 months | 14.6 (12.2) | n/a | RPQ-13 at 12 months | 11.7 (11.3) | n/a | 93% of 375 | 88% at 6 months<br><br>57% at 12 months (policy initially No later FUp if GOSE 8) | 15 |
|                     | 3 months (N=348)                                                                                                                                             |                                                   | 6 months (N=305) |                                                                                                                                                                                  | 12 months (N=285)       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| PCS symptom domain  | Mean (SD)                                                                                                                                                    | % ≥ 1 symptom                                     | Mean (SD)        | % ≥ 1 symptom                                                                                                                                                                    | Mean (SD)               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| Total PCS symptoms  | 5.8 (5.8)                                                                                                                                                    | 74.7                                              | 7.3 (6.1)*       | 82.4                                                                                                                                                                             | 6.8 (6.0)               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| Physical symptoms   | 2.4 (2.6)                                                                                                                                                    | 67.0                                              | 2.9 (2.8)*       | 71.8                                                                                                                                                                             | 2.8 (2.8)               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| Cognitive symptoms  | 1.4 (1.6)                                                                                                                                                    | 49.4                                              | 1.7 (1.7)*       | 59.3                                                                                                                                                                             | 1.7 (1.7)               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| Emotional symptoms  | 1.1 (1.5)                                                                                                                                                    | 43.4                                              | 1.5 (1.5)*       | 56.7                                                                                                                                                                             | 1.3 (1.5)               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| Sleep symptoms      | 1.0 (1.1)                                                                                                                                                    | 50.2                                              | 1.3 (1.2)*       | 60.3                                                                                                                                                                             | 1.1 (1.2)               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| Outcome and time    | Mean (SD)                                                                                                                                                    | % with clinically poorer outcomes                 |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| GOSE at 3 months    | 6.9 (1.1)                                                                                                                                                    | 33.2                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| GOSE at 6 months    | 6.9 (1.0)                                                                                                                                                    | 33.8                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| GOSE at 12 months   | 7.1 (1.0)                                                                                                                                                    | 22.4                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| BSI-18 at 6 months  | 55.6 (10.7)                                                                                                                                                  | 29.6                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| BSI-18 at 12 months | 51.8 (11.1)                                                                                                                                                  | 21.1                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| SWLS at 6 months    | 20.3 (8.0)                                                                                                                                                   | 44.5                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| SWLS at 12 months   | 22.0 (8.2)                                                                                                                                                   | 40.3                                              |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| RPQ-13 at 6 months  | 14.6 (12.2)                                                                                                                                                  | n/a                                               |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |
| RPQ-13 at 12 months | 11.7 (11.3)                                                                                                                                                  | n/a                                               |                  |                                                                                                                                                                                  |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                  |                                                                |                   |                  |  |                   |                    |           |               |           |               |           |                    |           |      |            |      |           |                   |           |      |            |      |           |                    |           |      |            |      |           |                    |           |      |            |      |           |                |           |      |            |      |           |                  |           |                                   |                  |           |      |                  |           |      |                   |           |      |                    |             |      |                     |             |      |                  |            |      |                   |            |      |                    |             |     |                     |             |     |            |                                                                                   |    |

| Refere<br>nce    | Population                                                                                                                                                                                                                                                                                                          | Study Design                                                  |  | Outcomes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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           | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up                                                                                               | Quality<br>appraisal |
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                | Stratification of patients by CT findings resulted in a significant difference in GOSE score at 3 months, with a greater proportion of CT positive patients with worse scores ( p < 0.001). There was no significant difference in GOSE scores between CT-positive and CT-negative patients at 6 or 12 months. |                                                                              |                                                                                                                                                                       |                      |
| 13 <sup>13</sup> | 11 US level I trauma centres. Participants with mTBI (GCS13-15) enrolled February 26, 2014 to May 4, 2016, and OTCs recruited by August 8, 2018,<br><br><u>17 and over in age</u><br><br><u>Pre existing debilitating psychiatric or neurologic disease excluded. Non English speaking excluded in most centres</u> | Comparative prospective multicentre longitudinal cohort study |  | GOSE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 3-<br>months<br>, 6-<br>months<br>and 12-<br>months<br>followi<br>ng<br>injury | 1154 patients (85.5%) met the criteria for mTBI.<br><br>975 out come data at 2 weeks 87% GOSE<8<br><br>3 months (see figure) 64% GOSE<8<br><br>6 months (see figure) 60% GOSE<8<br><br>12 months (n=768) 53% GOSE<8<br><br>versus 768 12 months post-injury                                                    | 76% of 1154 mTBI<br><br><u>73% of 299 controlscontrols not-specified</u>     | <u>94% at 6Not-clear</u><br><u>975-at 2weeks,</u><br><u>86%768</u> at 12 months<br><br><u>91% at 6 months</u><br><u>240-at 2-weeks,</u><br><u>67%146</u> at 12 months | 16                   |
| 14 <sup>14</sup> | Recruitment two Johns Hopkins emergency departments in Baltimore.                                                                                                                                                                                                                                                   | Prospective Cohort Study                                      |  | Rivermead PostConcu<br>ssion<br>Questionn<br>aire (RPQ)<br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br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|                                                                                |                                                                                                                                                                                                                                                                                                                |                                                                              |                                                                                                                                                                       |                      |

| Reference        | Population                                                                                                                                                             | Study Design                     |                         | Outcomes                                                               | Time points and factors         | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal       |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-------------------------|------------------------------------------------------------------------|---------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------------|-------------------------|-------------------------|------|-------------------------|------------------------|------------------------|----------------|--|---|---|-------|----|-----|------------------------|-----------------------|------------------------|---------------|--|-------|---|-------|-----|-------|------------------------|------------------------|------------------------|----------------|--|-------|---|-------|-----|--|--|--|
|                  |                                                                                                                                                                        |                                  |                         |                                                                        |                                 | <p><b>Table 4.</b> Mixed effects logistic regression model on d<br/>tomized age effects.</p> <table><tr><th>Variable</th><th>Odds Ratio<sup>a</sup></th><th>Odds Ratio<sup>b</sup></th><th>Odds Ratio<sup>c</sup></th><th>Odds Ratio<sup>d</sup></th></tr><tr><td>GOSE</td><td>7.554<br/>(3.088–18.479)</td><td>0.035<br/>(0.006–0.206)</td><td>0.790<br/>(0.675–0.925)</td><td>0.8<br/>(0.592–</td></tr><tr><td></td><td>0</td><td>0</td><td>0.003</td><td>0.</td></tr><tr><td>RPQ</td><td>1.162<br/>(0.666–2.026)</td><td>.032<br/>(0.008–0.134)</td><td>0.931<br/>(0.831–1.042)</td><td>1.1<br/>(0.86–</td></tr><tr><td></td><td>0.598</td><td>0</td><td>0.212</td><td>0.3</td></tr><tr><td>PHQ-9</td><td>0.658<br/>(0.386–1.123)</td><td>0.100<br/>(0.028–0.357)</td><td>0.870<br/>(0.777–0.974)</td><td>1.2<br/>(0.967–</td></tr><tr><td></td><td>0.125</td><td>0</td><td>0.016</td><td>0.0</td></tr></table> <p>Values are 'Odds ratio (confidence interval) <i>p</i>-value.<br/><sup>a</sup>Odds of having the outcome given young.<br/><sup>b</sup>Difference in odds at baseline between old and young.<br/><sup>c</sup>Rate of change in odds ratio of having the outcome over<br/>for younger.<br/><sup>d</sup>Difference in rate of change in odds ratio between old and young.</p> | Variable                                                         | Odds Ratio <sup>a</sup>                                        | Odds Ratio <sup>b</sup> | Odds Ratio <sup>c</sup> | Odds Ratio <sup>d</sup> | GOSE | 7.554<br>(3.088–18.479) | 0.035<br>(0.006–0.206) | 0.790<br>(0.675–0.925) | 0.8<br>(0.592– |  | 0 | 0 | 0.003 | 0. | RPQ | 1.162<br>(0.666–2.026) | .032<br>(0.008–0.134) | 0.931<br>(0.831–1.042) | 1.1<br>(0.86– |  | 0.598 | 0 | 0.212 | 0.3 | PHQ-9 | 0.658<br>(0.386–1.123) | 0.100<br>(0.028–0.357) | 0.870<br>(0.777–0.974) | 1.2<br>(0.967– |  | 0.125 | 0 | 0.016 | 0.0 |  |  |  |
| Variable         | Odds Ratio <sup>a</sup>                                                                                                                                                | Odds Ratio <sup>b</sup>          | Odds Ratio <sup>c</sup> | Odds Ratio <sup>d</sup>                                                |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
| GOSE             | 7.554<br>(3.088–18.479)                                                                                                                                                | 0.035<br>(0.006–0.206)           | 0.790<br>(0.675–0.925)  | 0.8<br>(0.592–                                                         |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
|                  | 0                                                                                                                                                                      | 0                                | 0.003                   | 0.                                                                     |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
| RPQ              | 1.162<br>(0.666–2.026)                                                                                                                                                 | .032<br>(0.008–0.134)            | 0.931<br>(0.831–1.042)  | 1.1<br>(0.86–                                                          |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
|                  | 0.598                                                                                                                                                                  | 0                                | 0.212                   | 0.3                                                                    |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
| PHQ-9            | 0.658<br>(0.386–1.123)                                                                                                                                                 | 0.100<br>(0.028–0.357)           | 0.870<br>(0.777–0.974)  | 1.2<br>(0.967–                                                         |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
|                  | 0.125                                                                                                                                                                  | 0                                | 0.016                   | 0.0                                                                    |                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                  |                                                                |                         |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |
| 15 <sup>15</sup> | Patients 16–60<br><br>Admitted single site-<br>Ullevål University<br>hospital neurosurgical<br>department 2000-2001.<br><br>Within 48 hours of injury<br>and GCS13-15. | Retrospective<br>cohort<br>study |                         | Rivermead<br>Post<br>Concussion<br>Symptoms<br><br>Questionnaire (RPQ) | 3, 6<br>and<br><br>12<br>months | 1-year cohort with mild TBI (N 96), one died before the 3-<br>months follow-up and one before the 6-months follow-up. Of<br>the survivors, 28 subjects did not attend any follow-ups, and 16<br>subjects attended 3 months but not 6- and 12- months follow-<br>ups. 52 subjects attended all follow-up consultations.<br><br>Any new PCS symptom n(%)<br><br><b>3 months</b> 38 (73%) <b>6 months</b> 26 (50%) <b>12 months</b> 28 (54%)<br><br>23% worsening PCS between 3-12 months<br><br>Twenty-nine subjects met the post-concussion syndrome criteria<br>at 3 months, and 22 patients at 6 and 12 months.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 70% of 96<br>patients                                            | 78% at 12 months                                               | 10                      |                         |                         |      |                         |                        |                        |                |  |   |   |       |    |     |                        |                       |                        |               |  |       |   |       |     |       |                        |                        |                        |                |  |       |   |       |     |  |  |  |

| Reference                     | Population                                                                                                                                                                                                                                                                                                                                                                                                                          | Study Design             |                 | Outcomes                                       | Time points and factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-----------------|------------------------------------------------|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|-----------------|----------------|---------------------|--|--|--|--|-------------------------------|--|--|--|--|-------|---------|----------|---------|------|---------|---------|---------|---------|------|-----------------------------|--|--|--|--|-------|----------|----------|----------|------|---------|---------|---------|---------|------|----------------------------|--|--|--|--|-------|----------|----------|----------|------|---------|---------|---------|---------|------|-----------|----------------|-----------------|-----------------|----------------|------------------------|--------|--------|--------|------|-------------------------|--------|--------|--------|------|---------------------------|--------|--------|--------|------|-----------|--------------------------|----|
| 16 <sup>16</sup>              | <p>December 2005–November 2008</p> <p>moderate and severe TBI referred 2 rehab clinics in Norway.</p> <p>Moderate TBI was defined by Glasgow Coma Scale (GCS) of 9–12 and Loss of Consciousness (LOC) more than 30 minutes, but less than 6 hours. Patients with clinical features of mild TBI, but who had traumatic CT pathology were upgraded to moderate TBI. Severe TBI was defined by GCS of 8 and LOC more than 6 hours.</p> | Prospective cohort study |                 | Functional independence measure (FIM) and GOSE | 3, 12 and 24 months     | <p>Table III. Functional independence measure (FIM) across three time periods.</p> <table><thead><tr><th></th><th>3 months (±SD)</th><th>12 months (±SD)</th><th>24 months (±SD)</th><th><i>p</i> Value</th></tr></thead><tbody><tr><td colspan="5">Injury severity/FIM</td></tr><tr><td colspan="5">Moderate TBI (<i>n</i> = 15)</td></tr><tr><td>FIM-M</td><td>91 (±1)</td><td>88 (±11)</td><td>90 (±4)</td><td>0.84</td></tr><tr><td>FIM-COG</td><td>34 (±3)</td><td>34 (±5)</td><td>34 (±3)</td><td>0.95</td></tr><tr><td colspan="5">Severe TBI (<i>n</i> = 26)</td></tr><tr><td>FIM-M</td><td>80 (±21)</td><td>81 (±20)</td><td>82 (±18)</td><td>0.34</td></tr><tr><td>FIM-COG</td><td>29 (±9)</td><td>29 (±9)</td><td>28 (±9)</td><td>0.26</td></tr><tr><td colspan="5">Total TBI (<i>n</i> = 41)</td></tr><tr><td>FIM-M</td><td>84 (±17)</td><td>84 (±18)</td><td>85 (±15)</td><td>0.39</td></tr><tr><td>FIM-COG</td><td>31 (±8)</td><td>30 (±8)</td><td>30 (±8)</td><td>0.30</td></tr></tbody></table> <p>Values are given as mean if not otherwise specified. FIM-M, FIM Motor sub-score (best score 91); FIM-COG, FIM Cognitive sub-score (best score 35). <i>p</i>-values are given with Friedman Test. <i>n</i> = 41 due to 24 incomplete data-sets.</p> <p>Table IV. Glasgow Outcome Scale Extended (GOSE) scores across three time periods.</p> <table><thead><tr><th>TBI group</th><th>3 months (±SD)</th><th>12 months (±SD)</th><th>24 months (±SD)</th><th><i>p</i> Value</th></tr></thead><tbody><tr><td>Total (<i>n</i> = 52)</td><td>5 (±1)</td><td>6 (±2)</td><td>6 (±2)</td><td>0.00</td></tr><tr><td>Severe (<i>n</i> = 32)</td><td>5 (±2)</td><td>5 (±2)</td><td>6 (±2)</td><td>0.10</td></tr><tr><td>Moderate (<i>n</i> = 20)</td><td>5 (±1)</td><td>7 (±1)</td><td>7 (±1)</td><td>0.00</td></tr></tbody></table> <p>*If <i>p</i> value is less than 0.05, there is a statistically significant effect of time; there is a change in scores across the three different time periods. <i>n</i> = 52 due to 13 incomplete data-sets.</p> |                                                                  | 3 months (±SD)                                                 | 12 months (±SD)   | 24 months (±SD) | <i>p</i> Value | Injury severity/FIM |  |  |  |  | Moderate TBI ( <i>n</i> = 15) |  |  |  |  | FIM-M | 91 (±1) | 88 (±11) | 90 (±4) | 0.84 | FIM-COG | 34 (±3) | 34 (±5) | 34 (±3) | 0.95 | Severe TBI ( <i>n</i> = 26) |  |  |  |  | FIM-M | 80 (±21) | 81 (±20) | 82 (±18) | 0.34 | FIM-COG | 29 (±9) | 29 (±9) | 28 (±9) | 0.26 | Total TBI ( <i>n</i> = 41) |  |  |  |  | FIM-M | 84 (±17) | 84 (±18) | 85 (±15) | 0.39 | FIM-COG | 31 (±8) | 30 (±8) | 30 (±8) | 0.30 | TBI group | 3 months (±SD) | 12 months (±SD) | 24 months (±SD) | <i>p</i> Value | Total ( <i>n</i> = 52) | 5 (±1) | 6 (±2) | 6 (±2) | 0.00 | Severe ( <i>n</i> = 32) | 5 (±2) | 5 (±2) | 6 (±2) | 0.10 | Moderate ( <i>n</i> = 20) | 5 (±1) | 7 (±1) | 7 (±1) | 0.00 | 95% of 21 | 100% at 12 and 24 months | 10 |
|                               | 3 months (±SD)                                                                                                                                                                                                                                                                                                                                                                                                                      | 12 months (±SD)          | 24 months (±SD) | <i>p</i> Value                                 |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Injury severity/FIM           |                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |                 |                                                |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Moderate TBI ( <i>n</i> = 15) |                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |                 |                                                |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| FIM-M                         | 91 (±1)                                                                                                                                                                                                                                                                                                                                                                                                                             | 88 (±11)                 | 90 (±4)         | 0.84                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| FIM-COG                       | 34 (±3)                                                                                                                                                                                                                                                                                                                                                                                                                             | 34 (±5)                  | 34 (±3)         | 0.95                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Severe TBI ( <i>n</i> = 26)   |                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |                 |                                                |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| FIM-M                         | 80 (±21)                                                                                                                                                                                                                                                                                                                                                                                                                            | 81 (±20)                 | 82 (±18)        | 0.34                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| FIM-COG                       | 29 (±9)                                                                                                                                                                                                                                                                                                                                                                                                                             | 29 (±9)                  | 28 (±9)         | 0.26                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Total TBI ( <i>n</i> = 41)    |                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |                 |                                                |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| FIM-M                         | 84 (±17)                                                                                                                                                                                                                                                                                                                                                                                                                            | 84 (±18)                 | 85 (±15)        | 0.39                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| FIM-COG                       | 31 (±8)                                                                                                                                                                                                                                                                                                                                                                                                                             | 30 (±8)                  | 30 (±8)         | 0.30                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| TBI group                     | 3 months (±SD)                                                                                                                                                                                                                                                                                                                                                                                                                      | 12 months (±SD)          | 24 months (±SD) | <i>p</i> Value                                 |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Total ( <i>n</i> = 52)        | 5 (±1)                                                                                                                                                                                                                                                                                                                                                                                                                              | 6 (±2)                   | 6 (±2)          | 0.00                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Severe ( <i>n</i> = 32)       | 5 (±2)                                                                                                                                                                                                                                                                                                                                                                                                                              | 5 (±2)                   | 6 (±2)          | 0.10                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| Moderate ( <i>n</i> = 20)     | 5 (±1)                                                                                                                                                                                                                                                                                                                                                                                                                              | 7 (±1)                   | 7 (±1)          | 0.00                                           |                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |                                                                |                   |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |
| 17 <sup>17</sup>              | Single centre: Norway's largest Level I Trauma                                                                                                                                                                                                                                                                                                                                                                                      | Prospective              |                 | The Rivermead Post                             | 3 and 12 months         | <p>40 mTBI patients</p> <p>34 moderate TBI patients</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <p>100% of 40 mild</p> <p>97% of 42 moderate</p>                 | <p>12 months 82% mild</p> <p>100% moderate</p>                 | 9                 |                 |                |                     |  |  |  |  |                               |  |  |  |  |       |         |          |         |      |         |         |         |         |      |                             |  |  |  |  |       |          |          |          |      |         |         |         |         |      |                            |  |  |  |  |       |          |          |          |      |         |         |         |         |      |           |                |                 |                 |                |                        |        |        |        |      |                         |        |        |        |      |                           |        |        |        |      |           |                          |    |

| Refere<br>nce                                                                           | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Study Design                       |              | Outcomes                                                                                                                                                                                                          | Time<br>points<br>and<br>factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up            | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
|-----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|--|--|--|----------|--|--------------|--|--|----------|-----------|----------|-----------|------------------|----|----|----|----|--------------------------------|-------|-------|-------|-------|------------------------------------------|-------------|-------------|-------------|------|--------------------------------------------|-----------|-----------|-----------|-----|--|--|--|
|                                                                                         | <p>Centre, Oslo University<br/>Hospital, Ulleval.</p> <p>1th5 May 2005 to 14<br/>May 2007.</p> <p>TBI was defined as loss<br/>of consciousness or some<br/>period of post-traumatic<br/>amnesia (PTA), skull<br/>fracture or objective<br/>neurolo-<br/>gical findings.</p> <p>Inclusion criteria were:</p> <p>(a) 16–55 years of age;<br/>(b) admitted within 24<br/>hours of injury; (c)<br/>Computed Tomography<br/>(CT) scan of the brain<br/>performed within 24<br/>hours post-injury;</p> <p>(d) fluent Norwegian<br/>speakers; (e) no severe<br/>substance abuse; (f) no<br/>known prior psychiatric<br/>or brain pathology; and<br/>(g) no associated spinal<br/>cord injury.</p> | Cohort<br>Study                    |              | <p>Concussion<br/>Symptoms</p> <p>Questionn<br/>aire (RPQ)</p> <p>Hospital<br/>Anxiety<br/>and<br/>Depression<br/>Scalce<br/>(HADS)</p> <p>Galveston<br/>Orientatio<br/>n and<br/>Amnesia<br/>Test<br/>(GOAT)</p> | post-<br>injury.                 | <table><tr><td colspan="5">Table II. Post-concussion symptoms at 3 and 12 months post-injury for participants with</td></tr><tr><td></td><td colspan="2">Mild TBI</td><td colspan="2">Moderate TBI</td></tr><tr><td></td><td>3 months</td><td>12 months</td><td>3 months</td><td>12 months</td></tr><tr><td>No. participants</td><td>40</td><td>33</td><td>34</td><td>33</td></tr><tr><td>Presence of PCS<sup>b</sup>*</td><td>40.0%</td><td>27.3%</td><td>29.4%</td><td>27.3%</td></tr><tr><td>RPQ mean total score (SD)<sup>***</sup></td><td>20.8 (18.3)</td><td>15.9 (16.9)</td><td>17.0 (15.4)</td><td>15.6</td></tr><tr><td>HADS Anxiety mean score (SD)<sup>**</sup></td><td>6.9 (4.9)</td><td>5.4 (4.6)</td><td>4.9 (4.2)</td><td>4.6</td></tr></table> <p>PCS = Postconcussion syndrome; RPQ = Rivermead Post Concussion Symptoms Questionnaire; HADS = Hospital Anxiety and Depression Scale.</p> <p><sup>a</sup> Repeated-measures of ANOVA: significant time × severity effect.</p> <p><sup>b</sup> Chi-square: significant group differences at 3 months post-injury.</p> <p>*<i>p</i> &lt; 0.05; **<i>p</i> &lt; 0.01.</p> | Table II. Post-concussion symptoms at 3 and 12 months post-injury for participants with |                                                                         |                      |  |  |  | Mild TBI |  | Moderate TBI |  |  | 3 months | 12 months | 3 months | 12 months | No. participants | 40 | 33 | 34 | 33 | Presence of PCS <sup>b</sup> * | 40.0% | 27.3% | 29.4% | 27.3% | RPQ mean total score (SD) <sup>***</sup> | 20.8 (18.3) | 15.9 (16.9) | 17.0 (15.4) | 15.6 | HADS Anxiety mean score (SD) <sup>**</sup> | 6.9 (4.9) | 5.4 (4.6) | 4.9 (4.2) | 4.6 |  |  |  |
| Table II. Post-concussion symptoms at 3 and 12 months post-injury for participants with |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                    |              |                                                                                                                                                                                                                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
|                                                                                         | Mild TBI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                    | Moderate TBI |                                                                                                                                                                                                                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
|                                                                                         | 3 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 12 months                          | 3 months     | 12 months                                                                                                                                                                                                         |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
| No. participants                                                                        | 40                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 33                                 | 34           | 33                                                                                                                                                                                                                |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
| Presence of PCS <sup>b</sup> *                                                          | 40.0%                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 27.3%                              | 29.4%        | 27.3%                                                                                                                                                                                                             |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
| RPQ mean total score (SD) <sup>***</sup>                                                | 20.8 (18.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 15.9 (16.9)                        | 17.0 (15.4)  | 15.6                                                                                                                                                                                                              |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
| HADS Anxiety mean score (SD) <sup>**</sup>                                              | 6.9 (4.9)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 5.4 (4.6)                          | 4.9 (4.2)    | 4.6                                                                                                                                                                                                               |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                         |                                                                         |                      |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |
| 18 <sup>18</sup>                                                                        | Mild to Moderate TBI<br><br>Single Centre Level<br>trauma centre USA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Prospec<br>tive<br>Cohort<br>Study |              | TBI<br>Symptom<br>Checklist                                                                                                                                                                                       | 1 week<br><br>_1<br>month        | 33 participants included (follow-up to 12 months)<br><br>18 aged 21-64 years                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 100% of 33                                                                              | 100% at 6 and 12<br>months                                              | 9                    |  |  |  |          |  |              |  |  |          |           |          |           |                  |    |    |    |    |                                |       |       |       |       |                                          |             |             |             |      |                                            |           |           |           |     |  |  |  |

| Refere<br>nce                  | Population                                                                                                                                                                                                                                                                                                                                                                                                                        | Study Design                                                                           |             | Outcomes                                                                                                                                                            | Time<br>points<br>and<br>factors                   | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up                    | Quality<br>appraisal |              |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|----------------------|--------------|--|----------|--|----------|--|--------|--|--|-------------|-----------|-------------|-----------|-------------|-----------|-------------|-----------|-------------|-----------|-------------------|--|--|--|--|--|--|--|--|--|--|-------|--|--|--|--|-----------|------------|-----------|------------|-----------|-------------|-----|--|--|--|--|-----------|-------------|-----------|-------------|-----------|--------------|--------------------------------|--|--|--|--|--|--|--|--|--|--|-------------|-------------|---------------|-------------|--------------|-------------|--------------|------------|---------------|-------------|--------------|-------------|-------------|-------------|------------|-------------|------------|------------|------------|------------|------------|-------------|--|--|--|
|                                | (Harborview Medical<br>Centre).<br><br>Inclusion criteria:<br><br>1) Arrival in the ED within<br>24 hours of<br><br>injury, 2) primary<br>diagnosis of TBI, 3) Initial<br>GCS s 9–15.<br><br>Exclusion criteria: 1)<br>cervical spinal cord<br><br>injury, 2) lower extremity<br>fracture, 3) prior history<br>of TBI, stroke or<br>dementia, 4)<br><br>hospitalization within the<br>past 6 months, 5) non-<br>English speaking. |                                                                                        |             | Functional<br>Status<br>Examinatio<br>n (FSE)<br><br>Glasgow<br>Outcome<br>Scale-<br>Extended<br>(GOS-E)<br><br>Health-<br>related<br>Quality of<br>Life<br>(HRQOL) | 3<br>months<br><br>6<br>months<br><br>12<br>months | 15 aged >64 years<br><br>Functional Status Ratings and Health-related Quality of Life up to 1 year following TBI by Age group. Younger TBI n=18, Older TBI n=15<br>reported as mean (SD).<br><table><tr><th></th><th colspan="2">1 week</th><th colspan="2">1 month</th><th colspan="2">3 months</th><th colspan="2">6 months</th><th colspan="2">1 year</th></tr><tr><th></th><th>Younger TBI</th><th>Older TBI</th><th>Younger TBI</th><th>Older TBI</th><th>Younger TBI</th><th>Older TBI</th><th>Younger TBI</th><th>Older TBI</th><th>Younger TBI</th><th>Older TBI</th></tr><tr><td colspan="11">Functional Status</td></tr><tr><td>GOS-E</td><td></td><td></td><td></td><td></td><td>6.9 (1.4)</td><td>5.1 (2.3)*</td><td>7.3 (1.4)</td><td>5.2 (2.4)*</td><td>7.2 (1.5)</td><td>4.6 (2.1)**</td></tr><tr><td>FSE</td><td></td><td></td><td></td><td></td><td>4.4 (6.0)</td><td>11.0 (8.7)*</td><td>3.4 (5.6)</td><td>10.3 (8.6)*</td><td>3.5 (5.3)</td><td>11.8 (7.0)**</td></tr><tr><td colspan="11">Health Related Quality of Life</td></tr><tr><td>SF-12v2 PCS</td><td>43.6 (12.2)</td><td>34.0 (15.2)**</td><td>41.7 (10.1)</td><td>32.8 (9.3)**</td><td>50.0 (14.2)</td><td>40.5 (10.6)*</td><td>51.1 (9.2)</td><td>36.3 (10.9)**</td><td>50.5 (11.7)</td><td>33.3 (9.3)**</td></tr><tr><td>SF-12v2 MCS</td><td>47.6 (10.1)</td><td>47.1 (15.1)</td><td>52.6 (7.6)</td><td>46.6 (12.3)</td><td>48.8 (6.5)</td><td>51.8 (9.7)</td><td>49.9 (6.5)</td><td>55.0 (7.2)</td><td>49.1 (7.0)</td><td>56.0 (9.3)*</td></tr></table><br>*<br>p<0.05,<br>**<br>p<0.01 |                                                                              | 1 week                                                                                     |                      | 1 month      |  | 3 months |  | 6 months |  | 1 year |  |  | Younger TBI | Older TBI | Younger TBI | Older TBI | Younger TBI | Older TBI | Younger TBI | Older TBI | Younger TBI | Older TBI | Functional Status |  |  |  |  |  |  |  |  |  |  | GOS-E |  |  |  |  | 6.9 (1.4) | 5.1 (2.3)* | 7.3 (1.4) | 5.2 (2.4)* | 7.2 (1.5) | 4.6 (2.1)** | FSE |  |  |  |  | 4.4 (6.0) | 11.0 (8.7)* | 3.4 (5.6) | 10.3 (8.6)* | 3.5 (5.3) | 11.8 (7.0)** | Health Related Quality of Life |  |  |  |  |  |  |  |  |  |  | SF-12v2 PCS | 43.6 (12.2) | 34.0 (15.2)** | 41.7 (10.1) | 32.8 (9.3)** | 50.0 (14.2) | 40.5 (10.6)* | 51.1 (9.2) | 36.3 (10.9)** | 50.5 (11.7) | 33.3 (9.3)** | SF-12v2 MCS | 47.6 (10.1) | 47.1 (15.1) | 52.6 (7.6) | 46.6 (12.3) | 48.8 (6.5) | 51.8 (9.7) | 49.9 (6.5) | 55.0 (7.2) | 49.1 (7.0) | 56.0 (9.3)* |  |  |  |
|                                | 1 week                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                        | 1 month     |                                                                                                                                                                     | 3 months                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 6 months                                                                     |                                                                                            | 1 year               |              |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
|                                | Younger TBI                                                                                                                                                                                                                                                                                                                                                                                                                       | Older TBI                                                                              | Younger TBI | Older TBI                                                                                                                                                           | Younger TBI                                        | Older TBI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Younger TBI                                                                  | Older TBI                                                                                  | Younger TBI          | Older TBI    |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| Functional Status              |                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                        |             |                                                                                                                                                                     |                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                                            |                      |              |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| GOS-E                          |                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                        |             |                                                                                                                                                                     | 6.9 (1.4)                                          | 5.1 (2.3)*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 7.3 (1.4)                                                                    | 5.2 (2.4)*                                                                                 | 7.2 (1.5)            | 4.6 (2.1)**  |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| FSE                            |                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                        |             |                                                                                                                                                                     | 4.4 (6.0)                                          | 11.0 (8.7)*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 3.4 (5.6)                                                                    | 10.3 (8.6)*                                                                                | 3.5 (5.3)            | 11.8 (7.0)** |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| Health Related Quality of Life |                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                        |             |                                                                                                                                                                     |                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                                            |                      |              |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| SF-12v2 PCS                    | 43.6 (12.2)                                                                                                                                                                                                                                                                                                                                                                                                                       | 34.0 (15.2)**                                                                          | 41.7 (10.1) | 32.8 (9.3)**                                                                                                                                                        | 50.0 (14.2)                                        | 40.5 (10.6)*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 51.1 (9.2)                                                                   | 36.3 (10.9)**                                                                              | 50.5 (11.7)          | 33.3 (9.3)** |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| SF-12v2 MCS                    | 47.6 (10.1)                                                                                                                                                                                                                                                                                                                                                                                                                       | 47.1 (15.1)                                                                            | 52.6 (7.6)  | 46.6 (12.3)                                                                                                                                                         | 48.8 (6.5)                                         | 51.8 (9.7)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 49.9 (6.5)                                                                   | 55.0 (7.2)                                                                                 | 49.1 (7.0)           | 56.0 (9.3)*  |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |
| 19 <sup>19</sup>               | Mild to moderate TBI<br><br>April 2017 and October<br>2018 5 hospitals in the<br><br>Netherlands.<br><br>Inclusion criteria:                                                                                                                                                                                                                                                                                                      | multice<br>nter,<br>prospec<br>tive,<br>longitud<br>inal<br>observa<br>tional<br>study |             | EuroQol-<br>5D-5L<br><br>Hospital<br>Anxiety<br>and<br>Depression<br>Scale<br>(HADS)                                                                                | 3, 6 &<br>12<br>months<br>from<br>injury           | A total of 230 cases were included for analyses of whom 182<br>(79%) sufered from mTBI and 48 (21%) from minor stroke.<br><br>Twenty-two cases did not complete all follow-up assessments.<br><br>See Figure 4: EQ5D5L separate outcome trajectories for<br>moderate or mTBI v stroke                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 96% of 230<br>enrolled at 6<br>weeks                                         | Not clear for mTBI<br>v stroke<br><br>91% and 90% of<br>total cohort at 6<br>and 12 months | 13                   |              |  |          |  |          |  |        |  |  |             |           |             |           |             |           |             |           |             |           |                   |  |  |  |  |  |  |  |  |  |  |       |  |  |  |  |           |            |           |            |           |             |     |  |  |  |  |           |             |           |             |           |              |                                |  |  |  |  |  |  |  |  |  |  |             |             |               |             |              |             |              |            |               |             |              |             |             |             |            |             |            |            |            |            |            |             |  |  |  |

| Reference        | Population                                                                                                                                                                                                                                                                                                                                                                                                                                    | Study Design                                              |  | Outcomes                                                                                                                         | Time points and factors | Results                                                              | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|--|----------------------------------------------------------------------------------------------------------------------------------|-------------------------|----------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|
|                  | <p>&gt;18 years of age) who suffered from TBI, stroke or other forms of acquired brain injury of mild to moderate severity as diagnosed by a clinician, within the past 6 weeks and were discharged home after visiting the emergency department (ED) or hospital admission.</p> <p>Exclusion criteria:</p> <p>legally incompetent, unable to follow up for 1 year or unable to complete questionnaires due lack of Dutch language skills</p> |                                                           |  |                                                                                                                                  |                         |                                                                      |                                                                  |                                                                |                   |
| 20 <sup>20</sup> | <p>Subset of multi- CENTER-TBI study</p> <p>Recruitment 19 December 2014 and 17 December 2017 Europe and Israel.</p> <p>mTBI (GCS 13–15) (underwent CT imaging for head injury)</p>                                                                                                                                                                                                                                                           | <p>Multi-centre prospective longitudinal cohort study</p> |  | <p>Short Form 36 Health Survey (SF36); Physical Component Score (PCS) and Mental Component Score (MCS)</p> <p>Post Traumatic</p> | <p>3 and 6 months</p>   | <p>1104 total 569 (51.5%) uncomplicated; 535 (48.5%) complicated</p> | <p>48% of 2277mTBI aged &gt;15 GOSE&gt;3</p>                     | <p>100% of cohort at 6 months as per eligibility criteria</p>  | <p>17</p>         |

| Refere<br>nce | Population                                                                                                                                                                                                | Study Design                 |                            | Outcomes                                                                                                                                                                                            | Time<br>points<br>and<br>factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal         |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|------------------------------|----------------------------|-----------|-----|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|----|-----|-------|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|----|-----|---------|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|--|--|--|
|               | <p>with GOSE &gt; 3 and complete outcomes in all instruments</p> <p>Comparison of complicated (injury on CT imaging) and uncomplicated mTBI</p> <p>Excluding people with prior neurological disorders</p> |                              |                            | <p>Stress Disorder Checklist PCL 5</p> <p>Extended Glasgow Outcome Scale (GOSE)</p> <p>Quality of Life After Brain Injury (QoLIBRI)</p> <p>Generalise d Anxiety Disorder Questionn aire (GAD-7)</p> |                                  | <p>Table 2. Percentages of impaired individuals according to the respective cut-off values.</p> <table><tr><th>Outcome</th><th>Time Points</th><th>Uncomplicated mTBI (n = 569)</th><th>Complicated mTBI (n = 535)</th></tr><tr><td rowspan="2">SF-36 PCS</td><td>3mo</td><td>24%</td><td>29%</td></tr><tr><td>6mo</td><td>21%</td><td>22%</td></tr><tr><td rowspan="2">SF-36 MCS</td><td>3mo</td><td>22%</td><td>30%</td></tr><tr><td>6mo</td><td>21%</td><td>28%</td></tr><tr><td rowspan="2">PCL-5</td><td>3mo</td><td>10%</td><td>10%</td></tr><tr><td>6mo</td><td>8%</td><td>10%</td></tr><tr><td rowspan="2">PHQ-9</td><td>3mo</td><td>16%</td><td>19%</td></tr><tr><td>6mo</td><td>16%</td><td>16%</td></tr><tr><td rowspan="2">GAD-7</td><td>3mo</td><td>11%</td><td>13%</td></tr><tr><td>6mo</td><td>8%</td><td>11%</td></tr><tr><td rowspan="2">QOLIBRI</td><td>3mo</td><td>19%</td><td>26%</td></tr><tr><td>6mo</td><td>19%</td><td>21%</td></tr><tr><td rowspan="2">GOSE</td><td>3mo</td><td>23%</td><td>41%</td></tr><tr><td>6mo</td><td>16%</td><td>35%</td></tr></table> <p>Abbreviations: mTBI = mild traumatic brain injury; 3mo = 3 months; 6mo = 6 months; SF-PCS = Short (36) Health Survey (physical component score); SF-MCS = Short Form (36) Health Survey (mental com score); PCL-5 = Posttraumatic Stress Disorder Checklist; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder questionnaire; QOLIBRI = Quality of Life after Brain Injury; GOSE = Glasgow Outcome Scale—Extended; n = number of cases. Note. Cut-off values: SF-36 PCS and SF-36 MCS &lt; 40, PCL-5 &lt; 10, PHQ-9 ≥ 10, GAD-7 ≥ 10, QOLIBRI &lt; 60, GOSE ≤ 6.</p> | Outcome                                                                      | Time Points                                                             | Uncomplicated mTBI (n = 569) | Complicated mTBI (n = 535) | SF-36 PCS | 3mo | 24% | 29% | 6mo | 21% | 22% | SF-36 MCS | 3mo | 22% | 30% | 6mo | 21% | 28% | PCL-5 | 3mo | 10% | 10% | 6mo | 8% | 10% | PHQ-9 | 3mo | 16% | 19% | 6mo | 16% | 16% | GAD-7 | 3mo | 11% | 13% | 6mo | 8% | 11% | QOLIBRI | 3mo | 19% | 26% | 6mo | 19% | 21% | GOSE | 3mo | 23% | 41% | 6mo | 16% | 35% |  |  |  |
| Outcome       | Time Points                                                                                                                                                                                               | Uncomplicated mTBI (n = 569) | Complicated mTBI (n = 535) |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| SF-36 PCS     | 3mo                                                                                                                                                                                                       | 24%                          | 29%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 21%                          | 22%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| SF-36 MCS     | 3mo                                                                                                                                                                                                       | 22%                          | 30%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 21%                          | 28%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| PCL-5         | 3mo                                                                                                                                                                                                       | 10%                          | 10%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 8%                           | 10%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| PHQ-9         | 3mo                                                                                                                                                                                                       | 16%                          | 19%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 16%                          | 16%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| GAD-7         | 3mo                                                                                                                                                                                                       | 11%                          | 13%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 8%                           | 11%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| QOLIBRI       | 3mo                                                                                                                                                                                                       | 19%                          | 26%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 19%                          | 21%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
| GOSE          | 3mo                                                                                                                                                                                                       | 23%                          | 41%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |
|               | 6mo                                                                                                                                                                                                       | 16%                          | 35%                        |                                                                                                                                                                                                     |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                              |                            |           |     |     |     |     |     |     |           |     |     |     |     |     |     |       |     |     |     |     |    |     |       |     |     |     |     |     |     |       |     |     |     |     |    |     |         |     |     |     |     |     |     |      |     |     |     |     |     |     |  |  |  |

| Refere<br>nce     | Population                                                                                                                                                                                                                                                                                                       | Study Design                       |       | Outcomes                                                                 | Time<br>points<br>and<br>factors                                                                                                                             | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal            |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|-------|--------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------|------------|-------------------------------|-------------|---------------|-------------|-----------|-------------|---------------|-------------|-------------------|-------|----------|------------|--------------|-------------|---------------|-------------|-----------|-------------|---------------|-------------|-----------------------------------|------------------------|-------|-----|-------|-------|-------|-------|-------|-----|-------|-------|-------|-------|-----|-------|-------|-------|-------|-------|-----|------|------|------|------|-----|------|------|------|------|-------|-----|------|------|------|------|-----|------|------|------|------|---------|-----|-------|-------|-------|-------|-----|-------|-------|-------|-------|------|-----|------|------|------|------|-----|------|------|------|------|--|--|--|
|                   |                                                                                                                                                                                                                                                                                                                  |                                    |       |                                                                          |                                                                                                                                                              | <div>Table A1. Descriptive statistics on outcomes by uncomplicated and complicated mTBI groups</div> <table><thead><tr><th rowspan="2">Outcome</th><th rowspan="2">Time Points</th><th colspan="2">Uncomplicated mTBI<br/>(n = 569)</th><th colspan="2">Complicated mTBI<br/>(n = 535)</th></tr><tr><th>M</th><th>SD</th><th>M</th><th>SD</th></tr></thead><tbody><tr><td rowspan="2">SF-36 PCS</td><td>3mo</td><td>47.41</td><td>10.56</td><td>45.56</td><td>10.56</td></tr><tr><td>6mo</td><td>48.58</td><td>10.37</td><td>47.59</td><td>10.37</td></tr><tr><td rowspan="2">SF-36 MCS</td><td>3mo</td><td>48.24</td><td>10.89</td><td>45.98</td><td>12.33</td></tr><tr><td>6mo</td><td>48.62</td><td>11.12</td><td>47.24</td><td>11.12</td></tr><tr><td rowspan="2">PCL-5</td><td>3mo</td><td>11.80</td><td>13.00</td><td>13.33</td><td>13.33</td></tr><tr><td>6mo</td><td>10.45</td><td>12.39</td><td>12.42</td><td>13.33</td></tr><tr><td rowspan="2">PHQ-9</td><td>3mo</td><td>4.69</td><td>4.90</td><td>5.17</td><td>5.17</td></tr><tr><td>6mo</td><td>4.40</td><td>4.92</td><td>4.84</td><td>5.17</td></tr><tr><td rowspan="2">GAD-7</td><td>3mo</td><td>3.35</td><td>4.25</td><td>3.77</td><td>4.25</td></tr><tr><td>6mo</td><td>3.15</td><td>4.02</td><td>3.61</td><td>4.02</td></tr><tr><td rowspan="2">QOLIBRI</td><td>3mo</td><td>74.77</td><td>16.46</td><td>70.79</td><td>17.18</td></tr><tr><td>6mo</td><td>75.17</td><td>17.18</td><td>72.32</td><td>17.18</td></tr><tr><td rowspan="2">GOSE</td><td>3mo</td><td>7.17</td><td>1.10</td><td>6.53</td><td>1.10</td></tr><tr><td>6mo</td><td>7.30</td><td>1.06</td><td>6.73</td><td>1.06</td></tr></tbody></table> <div>Abbreviations. mTBI = mild traumatic brain injury; 3mo = 3 months; 6mo = 6 months; SF-PCS = Short Form 36 Health Survey (physical component score); SF-MCS = Short Form (36) Health Survey (mental component score); PCL-5 = Posttraumatic Stress Disorder Checklist; PHQ-9 = Patient Health Questionnaire; GAD-7 = General Anxiety Disorder questionnaire; QOLIBRI = Quality of Life after Brain Injury; GOSE = Glasgow Outcome Scale—Extended; n = number of cases; M = mean; SD = standard deviation.</div> | Outcome                                                                      | Time Points                                                             | Uncomplicated mTBI<br>(n = 569) |            | Complicated mTBI<br>(n = 535) |             | M             | SD          | M         | SD          | SF-36 PCS     | 3mo         | 47.41             | 10.56 | 45.56    | 10.56      | 6mo          | 48.58       | 10.37         | 47.59       | 10.37     | SF-36 MCS   | 3mo           | 48.24       | 10.89                             | 45.98                  | 12.33 | 6mo | 48.62 | 11.12 | 47.24 | 11.12 | PCL-5 | 3mo | 11.80 | 13.00 | 13.33 | 13.33 | 6mo | 10.45 | 12.39 | 12.42 | 13.33 | PHQ-9 | 3mo | 4.69 | 4.90 | 5.17 | 5.17 | 6mo | 4.40 | 4.92 | 4.84 | 5.17 | GAD-7 | 3mo | 3.35 | 4.25 | 3.77 | 4.25 | 6mo | 3.15 | 4.02 | 3.61 | 4.02 | QOLIBRI | 3mo | 74.77 | 16.46 | 70.79 | 17.18 | 6mo | 75.17 | 17.18 | 72.32 | 17.18 | GOSE | 3mo | 7.17 | 1.10 | 6.53 | 1.10 | 6mo | 7.30 | 1.06 | 6.73 | 1.06 |  |  |  |
| Outcome           | Time Points                                                                                                                                                                                                                                                                                                      | Uncomplicated mTBI<br>(n = 569)    |       | Complicated mTBI<br>(n = 535)                                            |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   |                                                                                                                                                                                                                                                                                                                  | M                                  | SD    | M                                                                        | SD                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| SF-36 PCS         | 3mo                                                                                                                                                                                                                                                                                                              | 47.41                              | 10.56 | 45.56                                                                    | 10.56                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 48.58                              | 10.37 | 47.59                                                                    | 10.37                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| SF-36 MCS         | 3mo                                                                                                                                                                                                                                                                                                              | 48.24                              | 10.89 | 45.98                                                                    | 12.33                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 48.62                              | 11.12 | 47.24                                                                    | 11.12                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| PCL-5             | 3mo                                                                                                                                                                                                                                                                                                              | 11.80                              | 13.00 | 13.33                                                                    | 13.33                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 10.45                              | 12.39 | 12.42                                                                    | 13.33                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| PHQ-9             | 3mo                                                                                                                                                                                                                                                                                                              | 4.69                               | 4.90  | 5.17                                                                     | 5.17                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 4.40                               | 4.92  | 4.84                                                                     | 5.17                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| GAD-7             | 3mo                                                                                                                                                                                                                                                                                                              | 3.35                               | 4.25  | 3.77                                                                     | 4.25                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 3.15                               | 4.02  | 3.61                                                                     | 4.02                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| QOLIBRI           | 3mo                                                                                                                                                                                                                                                                                                              | 74.77                              | 16.46 | 70.79                                                                    | 17.18                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 75.17                              | 17.18 | 72.32                                                                    | 17.18                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| GOSE              | 3mo                                                                                                                                                                                                                                                                                                              | 7.17                               | 1.10  | 6.53                                                                     | 1.10                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
|                   | 6mo                                                                                                                                                                                                                                                                                                              | 7.30                               | 1.06  | 6.73                                                                     | 1.06                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| 21 <sup>21</sup>  | <div>Track TBI pilot study:<br/>three U.S. Level I trauma<br/>centres</div> <div>Initial GCS 13-15</div> <div>age ≥16-years, external<br/>force head trauma,<br/>presentation to enrolling<br/>centre, and clinically-</div> <div>indicated head computed<br/>tomography (CT) scan<br/>&lt;24 h of injury.</div> | Prospec<br>tive<br>cohort<br>study |       | <div>GOSE</div> <div>Acute<br/>Concussion<br/>Evaluation<br/>(ACE)</div> | <div>Outco<br/>me<br/>measur<br/>es<br/>were<br/>collecte<br/>d<br/>throug<br/>h in-<br/>person<br/>or<br/>phone</div> <div>interview at 3-<br/>and 6-</div> | <div>260 mTBI patients</div> <table><thead><tr><th colspan="2">3-MONTHS OUTCOMES</th></tr></thead><tbody><tr><td>GOSE ≤ 6</td><td>80 (30.8%)</td></tr><tr><td>ACE physical</td><td>2.33 ± 2.56</td></tr><tr><td>ACE cognitive</td><td>0.94 ± 1.10</td></tr><tr><td>ACE sleep</td><td>1.38 ± 1.65</td></tr><tr><td>ACE emotional</td><td>1.05 ± 1.45</td></tr><tr><th colspan="2">6-MONTHS OUTCOMES</th></tr><tr><td>GOSE ≤ 6</td><td>80 (30.8%)</td></tr><tr><td>ACE physical</td><td>2.84 ± 2.74</td></tr><tr><td>ACE cognitive</td><td>1.22 ± 1.18</td></tr><tr><td>ACE sleep</td><td>1.70 ± 1.69</td></tr><tr><td>ACE emotional</td><td>1.42 ± 1.52</td></tr></tbody></table> <div>ACE, Acute Concussion Evaluation; CT, computed tomography; ED, emergency department; GCS, Glasgow Coma Scale; GOSE, Glasgow Outcome Scale Extended; ICU, intensive care unit; SD, standard deviation.</div> <div>Multivariable analysis at 3-months:</div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 3-MONTHS OUTCOMES                                                            |                                                                         | GOSE ≤ 6                        | 80 (30.8%) | ACE physical                  | 2.33 ± 2.56 | ACE cognitive | 0.94 ± 1.10 | ACE sleep | 1.38 ± 1.65 | ACE emotional | 1.05 ± 1.45 | 6-MONTHS OUTCOMES |       | GOSE ≤ 6 | 80 (30.8%) | ACE physical | 2.84 ± 2.74 | ACE cognitive | 1.22 ± 1.18 | ACE sleep | 1.70 ± 1.69 | ACE emotional | 1.42 ± 1.52 | 100%<br>(retrospective<br>cohort) | 100% 3 and 6<br>months | 16    |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| 3-MONTHS OUTCOMES |                                                                                                                                                                                                                                                                                                                  |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| GOSE ≤ 6          | 80 (30.8%)                                                                                                                                                                                                                                                                                                       |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE physical      | 2.33 ± 2.56                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE cognitive     | 0.94 ± 1.10                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE sleep         | 1.38 ± 1.65                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE emotional     | 1.05 ± 1.45                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| 6-MONTHS OUTCOMES |                                                                                                                                                                                                                                                                                                                  |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| GOSE ≤ 6          | 80 (30.8%)                                                                                                                                                                                                                                                                                                       |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE physical      | 2.84 ± 2.74                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE cognitive     | 1.22 ± 1.18                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE sleep         | 1.70 ± 1.69                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |
| ACE emotional     | 1.42 ± 1.52                                                                                                                                                                                                                                                                                                      |                                    |       |                                                                          |                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                              |                                                                         |                                 |            |                               |             |               |             |           |             |               |             |                   |       |          |            |              |             |               |             |           |             |               |             |                                   |                        |       |     |       |       |       |       |       |     |       |       |       |       |     |       |       |       |       |       |     |      |      |      |      |     |      |      |      |      |       |     |      |      |      |      |     |      |      |      |      |         |     |       |       |       |       |     |       |       |       |       |      |     |      |      |      |      |     |      |      |      |      |  |  |  |

| Reference | Population                                 | Study Design | Outcomes | Time points and factors | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |
|-----------|--------------------------------------------|--------------|----------|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|
|           | Convenience sampling from years 2010–2012. |              |          | months                  | <p>psychiatric history predictor of functional disability (GOSE<math>\leq</math>6: OR = 2.75, 95% CI [1.44–5.27]) and all domains of post-concussive symptoms (ACE-physical: B = 1.06 [0.38–1.73]; ACE-cognitive: B = 0.72 [0.26–1.17]; ACE-sleep: B = 0.46 [0.17–0.75]; ACE-emotional: B = 0.64 [0.25–1.03]).</p> <p>Headaches/migraine history predictor for functional disability (GOSE <math>\leq</math> 6: OR = 4.10 [1.67–10.07]), and sleep and emotional postconcussive symptoms (ACE-sleep: B = 0.57 [0.15–1.00]; ACE emotional: B = 0.92 [0.35–1.49]). Gastrointestinal history was a predictor for physical post-concussive symptoms (ACE-physical: B = 1.25 [0.41–2.10]).</p> <p>Multivariable analysis at 6-months, psychiatric history was a predictor for functional disability (GOSE <math>\leq</math> 6: OR = 2.57 [1.38–4.77]) and all domains of post-concussive symptoms (ACEphysical: B = 1.38 [0.68–2.09]; ACE-cognition: B = 0.74 [0.28–1.20]; ACE-sleep: B = 0.51 [0.20–0.83]; ACE-emotional: B = 0.93 [0.53–1.33]). Headache/migraine history was a predictor for</p> |                                                                  |                                                                |                   |

| Refere<br>nce    | Population                                                                                                                                                                                                                                                                                                                                             | Study Design                       |  | Outcomes                                                                                                               | Time<br>points<br>and<br>factors    | Results                                                                                                                                                                                                                                                                 | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up                                                             | Quality<br>appraisal |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--|------------------------------------------------------------------------------------------------------------------------|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|----------------------|
|                  |                                                                                                                                                                                                                                                                                                                                                        |                                    |  |                                                                                                                        |                                     | physical post-concussive symptoms (ACE-<br>physical: B = 1.81<br>[0.79–2.84]                                                                                                                                                                                            |                                                                              |                                                                                                                                     |                      |
| 22 <sup>22</sup> | Mild TBI patients<br>presenting to ED single<br>hospital Christchurch.<br><br>Age 15 or more                                                                                                                                                                                                                                                           | Prospec<br>tive<br>cohort<br>study |  | Rivermead<br>Post-<br>concussion<br>Symptoms<br>Questionn<br>aire<br><br>Eye<br>movement<br>s<br><br>Motor<br>deficits | 1 week,<br>3, 6<br>and 12<br>months | N=37<br><br>1 week RPSQ mean score 19.81 ± 11.72<br><br>3 months RPSQ mean score 9.81 ± 9.89<br><br>6 months RPSQ mean 10.24 ± 10.65<br><br>12 months, RPSQ mean 10.13 ± 11.9                                                                                           | 100%                                                                         | 84%                                                                                                                                 | 14                   |
| 23 <sup>23</sup> | The Transforming<br>Research and Clinical<br>Knowledge in TBI<br>(TRACK-TBI) prospective<br>cohort study enrolled<br>2697 participants with<br>TBI at 18 U.S. level 1<br>trauma centers between<br>February 26, 2014 and<br>July 3, 2018. Participants<br>were evaluated at 2<br>weeks and 3, 6, and 12<br>months post-injury. All<br>TBI participants | Prospec<br>tive<br>cohort<br>study |  | Rivermead<br>Post-<br>concussion<br>Symptoms<br>Questionn<br>aire                                                      | 2 week,<br>3, 6<br>and 12<br>months | <b>2 weeks</b> n 1593<br><br>Total score Mean (SD) 18.4 (14.9) Median<br>(IQR) 15 (6, 28)<br><br>No of symptoms endorsed Mean (SD) 6.8 (4.8) Median<br>(IQR) 6 (3, 11)<br><br><b>3 months</b> n 1480<br><br>Total score Mean (SD) 14.2 (14.8) Median (IQR)<br>9 (2, 24) | 88% of<br>1681mTBI                                                           | 94% at 6 months<br>87% at 12 months<br><br>OTC 91% and<br>86% at 6 and 12<br>months<br><br>FC 100% and 93%<br>at 6 and 12<br>months | 18                   |

| Reference        | Population                                                                                                                                                                                                                                               | Study Design             |  | Outcomes                                                                                                                              | Time points and factors                         | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                        | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|--|---------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|
|                  | <p>sustained a TBI &lt;24 h before enrollment and received a CT head.GCS13-15</p> <p>219 orthopaedic trauma controls (OTC)</p> <p>275 Friend controls (FC)</p>                                                                                           |                          |  |                                                                                                                                       |                                                 | <p>No. endorsed 4 (1, 9)      Mean (SD) 5.3 (4.9)      Median (IQR)</p> <p><b>6 months</b>      n      1397</p> <p>Total score 8 (0, 0.50)      Mean (SD) 12.9 (14.6)      Median (IQR)</p> <p>No. endorsed 3 (0, 8)      Mean (SD) 4.9 (4.9)      Median (IQR)</p> <p><b>12 months</b>      n      1292</p> <p>Total score (0, 20)      Mean (SD) 12.2 (14.2)      Median (IQR) 6</p> <p>No. endorsed (0, 8)      Mean (SD) 4.6 (4.8)      Median (IQR) 3</p> |                                                                  |                                                                |                   |
| 24 <sup>24</sup> | <p>Adults 18 years or over Johns Hopkins Hospital or Johns Hopkins Bayview Medical Center emergency departments June 2014 through June 2017 underwent CT imaging for head trauma</p> <p>GCS13-15, <a href="#">loc &lt;30minutes, PTA&lt;24 hours</a></p> | Prospective cohort study |  | <p>Rivermead Post-concussion Symptoms Questionnaire</p> <p>Patient Health Questionnaire 9 item (PHQ-9)</p> <p>General Anxiety and</p> | <p>Baseline, 1-month, 3 months and 6 months</p> | <p>N=253</p> <p>RPQ scores <b>Baseline</b> Mean (SD) 14.22 (10.04)</p> <p><b>1-Month</b> 13.06 (11.89)</p> <p><b>3-Month</b> 12.34 (12.59)</p> <p><b>6-Month</b> 11.01 (12.91)</p> <p>Different trajectories 13.4% developed worsening symptoms over 12 months</p>                                                                                                                                                                                             | 81% of 310                                                       | 100% at 6 and 12 months                                        | 16                |

| Refere<br>nce    | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Study Design                       |  | Outcomes                                                                                                                                                                                                                             | Time<br>points<br>and<br>factors | Results                                                                                                                                                                                                                                                                                                                                                                                      | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
|                  | <p>Patient with findings CT<br/>excluded</p> <p>Also patients with prior<br/>intracranial pathology<br/>including dementia, non<br/>English speakers and<br/>those with no phone <u>and</u><br/><u>those who did not attend</u><br/><u>for 3 follow ups</u></p>                                                                                                                                                                                                             |                                    |  | <p>Depression<br/>Quesitonnn<br/>aire (GAD)</p> <p>PSQI</p> <p>SF-MPQ</p>                                                                                                                                                            |                                  |                                                                                                                                                                                                                                                                                                                                                                                              |                                                                              |                                                                         |                      |
| 25 <sup>25</sup> | <p>Aged ≥65 year, fluent in<br/>English, functionally<br/>independent.</p> <p>Recruited Alfred<br/>Hospital, Melbourne<br/>Australia</p> <p>January 2016 and March<br/>2019.</p> <p>mTBI blunt head trauma<br/>resulting in: (i)<br/>disorientation, (ii) loss of<br/>consciousness (LOC)<br/>≤30 minutes, (iii) post-<br/>traumatic amnesia (PTA)<br/>≤24 hours, and/or (iv)<br/>other transient<br/>neurological<br/>abnormalities (e.g.,<br/>intracranial lesion not</p> | Prospec<br>tive<br>cohort<br>study |  | <p>World<br/>Health<br/>Organisatio<br/>n Quality<br/>of Life<br/>Scale –<br/>shortened<br/>version<br/>(WHOQOL-<br/>BREF)</p> <p>Psychologi<br/>cal health<br/>(Depressio<br/>n, anxiety<br/>and stress<br/>scale;<br/>DASS-21)</p> | <p>3, 6<br/>months</p>           | <p>40 mTBI patients</p> <p><b>3-months</b></p> <p><b>6-months</b></p> <p>WHOQOL-BREF</p> <p>Physical      –0.40 (0.96)      Physical      –0.36<br/>(0.96)</p> <p>Psychological      –0.27 (0.98)      Psychological      –0.14<br/>(0.98)</p> <p>Social      –0.25 (0.98)      Social      –0.07<br/>(0.98)</p> <p>Environment      –0.11 (0.99)      Environment      –0.12<br/>(0.99)</p> | <p>75% of 142 mTBI<br/>and trauma<br/>patients<br/>approached</p>            | <p>All cohorts 100%<br/>at 6 months</p>                                 | 15                   |

| Refere<br>nce    | Population                                                                                                                                                                                                                                                                                                                                                          | Study Design                       |  | Outcomes                                                                                                        | Time<br>points<br>and<br>factors              | Results                                                                                                                                                                                                                                                                                                                                                                                                             | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--|-----------------------------------------------------------------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
|                  | <p>requiring surgery). Additionally, a Glasgow Coma Scale (GCS) score between 13 and 15 was recorded by 30 minutes postinjury or upon presentation to health services for treatment</p> <p>excluding prior dementia, intoxication and current therapy for psychiatric disorder</p> <p>66 age matched trauma controls</p> <p>47 age matched non injured controls</p> |                                    |  |                                                                                                                 |                                               | <p>QoL Sum -0.47 (0.97) QoL Sum -0.31</p> <p>DASS-21</p> <p>Psych Health 0.24 (0.99) Psych Health 0.09</p>                                                                                                                                                                                                                                                                                                          |                                                                              |                                                                         |                      |
| 26 <sup>26</sup> | <p>Single Centre Christchurch Hospital New Zealand</p> <p>GCS13-15 presenting within 24 hour of injury with loc &lt;20 minutes and PTA &lt; 24 hours</p> <p>Exclusion if abnormal CT scan, evidence of regular intake of psychoactive drugs or history of drug abuse, central neurological disorder or psychiatric condition,</p>                                   | Prospec<br>tive<br>Cohort<br>Study |  | <p>Fatigue Severity Scale (FSS)</p> <p>Rivermead Post-concussion Symptoms Questionnaire (RPSQ) Fatigue item</p> | <p>1 week</p> <p>3 months</p> <p>6 months</p> | <p>Prevalence (n)RPQ Severity FFS &gt;3.7(n)</p> <p><b>1 week</b> 68.1% (263) 54.9% (255)</p> <p><b>3 months</b> 31.4% (226) 37.6% (218)</p> <p><b>6 months</b> 28.2% (202) 34.4% (195)</p> <p>N=159 complete data</p> <p>RPSQ (Fatigue item) Mean(SD) FSSMean (SD) S F36v2 Vitality Mean(SD)</p> <p><b>1 week</b> 2.09(1.24) 3.99(1.53) 46.57(24.72)</p> <p><b>3 months</b> 1.03(1.05) 3.29(1.44) 60.21(19.68)</p> | 86% of 263 enrolled patients                                                 | 89% at 6 months                                                         | 13                   |

| Refere<br>nce    | Population                                                                                                                                                                                                                                                                                                                                                                                      | Study Design                       |  | Outcomes                                                                                                                                | Time<br>points<br>and<br>factors | Results                                                                                                                                                                                                                                                                                                                                                                            | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
|                  | evidence of skull or facial fractures or presence of multiple trauma or significant trauma to other parts of the body (e.g. broken limbs or ribs, spinal injuries, soft tissue injury requiring plastic surgery).                                                                                                                                                                               |                                    |  | Vitality scale of the Short Form 36 Health Survey– Version 2 (SF-36v2)<br><br>Hospital Anxiety and Depression Scale (HADS)              |                                  | <b>6 months</b> 0.96(1.05) 3.20 (1.39) 62.11(20.18)                                                                                                                                                                                                                                                                                                                                |                                                                              |                                                                         |                      |
| 27 <sup>27</sup> | Recruited two EDs in Baltimore: Johns Hopkins Bayview Medical Center, a level-2 trauma center, and Johns Hopkins Hospital, a level-1 trauma center. 18 years or older and presented to the ED within 24 hours of blunt head injury, met the American College of Emergency Physicians criteria for evaluation with an intracranial computerized tomography (CT) scan. Loc< 30minutes, PTA<24hour | Prospec<br>tive<br>cohort<br>study |  | Patient Health Questionnaire–9 (PHQ-9) depression symptoms<br><br>Rivermead Post-Concussion Questionnaire<br><br>Glasgow Outcome Scale– | 3 and 6 months                   | <b>At 3 or 6 months</b> n=49 depressive symptoms n=168 no depressive symptoms (PHQ>9)<br><br><b>3 months</b><br><br>Postconcussive symptoms (mean±SD)<br><br>No depressive symptoms 8.2 (8.7)Depressive symptoms 30.7 (15.2) <0.001<br><br>Functional recovery (GOSE =8)<br><br>No depressive symptoms<br><br>Incomplete 86 (50.6%) Complete 84 (49.4%)<br><br>Depressive symptoms | 73% of 278 enrolled                                                          | 83% of 217 at 6 months                                                  | 13                   |

| Refere<br>nce    | Population                                                                                                                                                                                                                                                                                                                                                 | Study Design                       |  | Outcomes                                                          | Time<br>points<br>and<br>factors  | Results                                                                                                                                                                                                                                                                                                                                                                                                          | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--|-------------------------------------------------------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
|                  | Initial GCS13-15<br><br>Consent for blood test<br><br>Patient previous brain<br>injury excluded excluding<br>those with prior<br>intracranial pathology<br>including dementia non<br>English speakers and<br>those with no phone                                                                                                                           |                                    |  | Extended<br>(GOSE)                                                |                                   | Incomplete 30 (96.8%) Complete 1.0<br>(3.2%) <0.001<br><br><b>6 months</b> Postconcussive symptoms (mean±SD)<br><br>No depressive symptoms 6.3 (8.0) Depressive symptoms 32.3<br>(14.6) <0.001<br><br>Functional recovery (GOSE =8)<br><br>No depressive symptoms<br><br>Incomplete 59 (39.9%) Complete 89<br>(60.1%)<br><br>Depressive symptoms<br><br>Incomplete 27 (93.1%) Complete 2 (6.9%)<br><0.001 <0.001 |                                                                              |                                                                         |                      |
| 28 <sup>28</sup> | Single Level 1 trauma<br>centre Seattle<br><br>CDC definition mTBI,<br>adults- divided into 21-54<br>and 55 and<br>over. Recruited within 24<br>hours of injury<br><br>excluding moderate<br>extracranial injury and 13<br>age matched uninjured<br>controls. Both excluding<br>those with prior history<br>of dementia, TBI or<br>stroke within past year | Prospec<br>tive<br>cohort<br>study |  | Rivermead<br>Post-<br>Concussion<br>Symptoms<br>Questionn<br>aire | 0, 3<br>months<br>and 6<br>months | 18 mTBI patients RPQ<br><br>11 older adults (55 and over) 7 younger adults<br><br>Day 0 25.1 ± 8.1 D 21.4 ± 9.1<br><br>3 months 18.0 ± 7.1 14.6 ± 4.8<br><br>6 months 17.1 ± 3.6 12.6 ± 3.5                                                                                                                                                                                                                      | Not clear                                                                    | 100% at 6 months                                                        | 13                   |

| Refere<br>nce     | Population                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Study Design                       |  | Outcomes                                                          | Time<br>points<br>and<br>factors                | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | % (n) of acute<br>injury<br>population<br>enrolled with 3<br>month follow up | % of 3 month<br>population with<br>six and/or twelve<br>month follow up | Quality<br>appraisal |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--|-------------------------------------------------------------------|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------|
| 29 <sup>29</sup>  | Single Level 1 trauma<br>centre USA<br><br>American Congress of<br>Rehabilitation Medicine<br>(ACRM) definition of<br>mTBI.<br><br>Recruited within 24<br>hours of injury<br><br>age >17 with either<br>positive CT brain scan,<br>LOC or PTA within 24<br>hours of injury excluding<br>pregnancy, being in<br>custody, non English<br>speaker, history of<br>serious psychiatric and<br>neurological disorder or<br>pre existing conditions<br>precluding follow up | Prospec<br>tive<br>cohort<br>study |  | Rivermead<br>Post-<br>Concussion<br>Symptoms<br>Questionn<br>aire | 2<br>weeks,<br>3<br>months<br>, and 6<br>months | N=171mTBI with any post acute follow up<br><br>Mean (SD) RPQ score: 17.96 (13.40) enrollment (< 24 hours of<br>injury),<br><br><b>2 weeks</b> , 17.62 (15.70)<br><br><b>3 months</b> , 11.73 (15.75)<br><br><b>6 months</b> .10.68 (14.48)<br><br>Higher neighborhood disadvantage associated with higher<br>symptom burden 3 and 6 months in multilevelmodelling.                                                                                                                                                             | 52% of 199<br>enrolled                                                       | 80% at 6 months                                                         | 13                   |
| 30. <sup>30</sup> | Age 60 and over with<br>mTBI defined as head<br>injury with either loc or<br>post traumatic amnesia<br><br>Exclusion criteria prior<br>history of any of the<br>conditions below<br><br>Prior substance use,<br>psychiatric conditions,<br>brain injury,<br>neurodegenerative<br>conditions, insufficient<br>dutch language, multiple<br>injuries (204/456), not<br>consenting or not                                                                                | Prospec<br>tive<br>cohort<br>study |  | GOSE <8                                                           | 3 and<br>6<br>months                            | <b>3 months</b><br><br>89 /154 GOSE<8 (57%)<br><br>Predicted by baseline factors of living situation, intracranial<br>injury HADS -D (hospital anxiety and depression scale) and HISC<br>(head injury symptoms checklist) at baseline in mv model of<br>demographic, comorbid and injury factors in multivariate model<br><br><b>6 months</b><br><br>69/146 GOSE<8 (47%)<br><br>28 of 89 with 3 month GOSE<8 improved<br><br>11 of 66 with 3 month GOSE =8 deteriorated<br><br>No significant predictors in multivariate model | 85% of 182<br>numerator<br>excluding 3<br>known deceased                     | 95% of 154<br>numerator<br>excluding 1<br>known deceased                | 19                   |

| Reference | Population                          | Study Design |  | Outcomes | Time points and factors | Results | % (n) of acute injury population enrolled with 3 month follow up | % of 3 month population with six and/or twelve month follow up | Quality appraisal |
|-----------|-------------------------------------|--------------|--|----------|-------------------------|---------|------------------------------------------------------------------|----------------------------------------------------------------|-------------------|
|           | contactable post discharge (70/456) |              |  |          |                         |         |                                                                  |                                                                |                   |

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Table III. Associations of age, IQ, years of education and measures of injury severity with the Rivermead Post-Concussion Symptoms Questionnaire (RPSQ), Rivermead Head-Injury Follow-up Questionnaire (RHIFQ) and Short-Form 36 Health Survey (SF-36) [table]; p. 618. [cited 2025 Mar 7]

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Table S4. Quality of the Studies Based on the Downs and Black Checklist

| Items                           |    | 1)Al Fauzi et al | 2)Candrian et al | 3 )Carrol et al | 4)Chakroun-Wealha et al | 5)Chiang et al | 6+7)Heitger et al (2007 studies) | 8) Heitger et 8 (2006 study) | 9)Karaliute et al | 10)Krauss et al | 11) Madhok et al | 12) McCreath et al | 13) McMah on et al | 14) Nelson et al |
|---------------------------------|----|------------------|------------------|-----------------|-------------------------|----------------|----------------------------------|------------------------------|-------------------|-----------------|------------------|--------------------|--------------------|------------------|
| Reporting                       | 1  | 1                | 1                | 1               | 1                       | 1              | 1                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
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|                                 | 3  | 1                | 1                | 1               | 1                       | 1              | 1                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 4  | 1                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 1                | 1                  | 1                  | 1                |
|                                 | 5  | 1                | 1                | 1               | 1                       | 0              | 0                                | 1                            | 0                 | 0               | 1                | 1                  | 1                  | 2                |
|                                 | 6  | 1                | 1                | 1               | 1                       | 1              | 1                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 7  | 0                | 0                | 0               | 0                       | 0              | 0                                | 1                            | 1                 | 0               | 0                | 0                  | 0                  | 1                |
|                                 | 8  | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 0                  | 0                  | 0                |
|                                 | 9  | 1                | 1                | 0               | 0                       | 1              | 1                                | 1                            | 0                 | 0               | 0                | 1                  | 1                  | 0                |
|                                 | 10 | 0                | 0                | 0               | 0                       | 0              | 0                                | 1                            | 0                 | 0               | 1                | 1                  | 0                  | 0                |
| External validity               | 11 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 0                  | 0                  | 0                |
|                                 | 12 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 1                  | 1                  | 1                |
|                                 | 13 | 0                | 0                | 0               | 0                       | 0              | 1                                | 0                            | 1                 | 1               | 0                | 0                  | 0                  | 1                |
| Internal validity - bias        | 14 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 1                | 0                  | 0                  | 0                |
|                                 | 15 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 0                  | 0                  | 0                |
|                                 | 16 | 1                | 1                | 1               | 1                       | 1              | 1                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 17 | 1                | 1                | 1               | 1                       | 1              | 0                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 18 | 1                | 1                | 1               | 1                       | 1              | 1                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 19 | 0                | 0                | 0               | 0                       | 0              | 1                                | 0                            | 1                 | 1               | 0                | 0                  | 0                  | 0                |
|                                 | 20 | 1                | 1                | 1               | 1                       | 1              | 1                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 21 | 1                | 1                | 1               | 1                       | 1              | 0                                | 1                            | 0                 | 1               | 0                | 0                  | 1                  | 1                |
| Internal validity - confounding | 22 | 1                | 1                | 1               | 1                       | 1              | 0                                | 1                            | 1                 | 1               | 1                | 1                  | 1                  | 1                |
|                                 | 23 | 1                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 0                  | 0                  | 0                |
|                                 | 24 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 0                  | 0                  | 0                |
|                                 | 25 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 0               | 0                | 0                  | 0                  | 0                |
|                                 | 26 | 1                | 1                | 1               | 1                       | 1              | 0                                | 0                            | 0                 | 0               | 0                | 1                  | 1                  | 0                |
|                                 | 27 | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 1               | 0                | 0                  | 0                  | 0                |
| Power                           |    | 0                | 0                | 0               | 0                       | 0              | 0                                | 0                            | 0                 | 1               | 0                | 0                  | 0                  | 0                |
| Total score                     |    | 15               | 13               | 12              | 12                      | 12             | 10                               | 14                           | 12                | 13              | 13               | 15                 | 15                 | 16               |

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| Items                                 |    | 15) Richey<br>et al | 16) Roe et<br>al | 17) Sandhau<br>g et al | 18) Sigurdardo<br>tti et al | 19) Thompso<br>n et al | 20)Voormolen<br>et al | 21) Verberne<br>et al | 22) Yue<br>et al | 23) Macha<br>mer et al | 24) Keatley<br>et al | 25) Hume<br>et al | 26) Norie<br>et al | 27) Roy<br>et al | 28) Martha<br>et al | 29) Miller et<br>al | 30) Thuss et<br>al |
|---------------------------------------|----|---------------------|------------------|------------------------|-----------------------------|------------------------|-----------------------|-----------------------|------------------|------------------------|----------------------|-------------------|--------------------|------------------|---------------------|---------------------|--------------------|
| Reporting                             | 1  | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 2  | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 3  | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 4  | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 5  | 1                   | 0                | 0                      | 0                           | 0                      | 2                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 6  | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 7  | 1                   | 0                | 0                      | 0                           | 0                      | 1                     | 0                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 8  | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
|                                       | 9  | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 1                  |
|                                       | 10 | 1                   | 1                | 1                      | 0                           | 0                      | 1                     | 0                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
| Exter<br>nal<br>validi<br>ty          | 11 | 0                   | 0                | 0                      | 0                           | 0                      | 1                     | 1                     | 1                | 1                      | 1                    | 0                 | 0                  | 0                | 0                   | 0                   | 1                  |
|                                       | 12 | 0                   | 0                | 0                      | 0                           | 0                      | 1                     | 0                     | 1                | 1                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
|                                       | 13 | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
| Internal validity<br>- bias           | 14 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
|                                       | 15 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
|                                       | 16 | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 17 | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 18 | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
|                                       | 19 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 0                  |
|                                       | 20 | 1                   | 1                | 1                      | 1                           | 1                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 1                  | 1                | 1                   | 1                   | 1                  |
| Internal<br>validity -<br>confounding | 21 | 1                   | 0                | 0                      | 0                           | 0                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 0                  | 0                | 0                   | 0                   | 1                  |
|                                       | 22 | 1                   | 0                | 0                      | 0                           | 0                      | 1                     | 1                     | 1                | 1                      | 1                    | 1                 | 0                  | 0                | 0                   | 0                   | 1                  |
|                                       | 23 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
|                                       | 24 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 0                  |
|                                       | 25 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 1                  |
|                                       | 26 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 1                  |
| Power                                 | 27 | 0                   | 0                | 0                      | 0                           | 0                      | 0                     | 0                     | 0                | 0                      | 0                    | 0                 | 0                  | 0                | 0                   | 0                   | 1                  |
| Total score                           |    | 14                  | 10               | 10                     | 9                           | 9                      | 17                    | 13                    | 16               | 18                     | 16                   | 15                | 13                 | 13               | 13                  | 13                  | 19                 |

Note: 2, criterion fully met (item 5); 1, criterion met or partially met (item 5); 0, criterion not met. Downs and Black checklist item descriptions: 1, hypothesis/aims/objectives reported; 2, main outcome measures reported; 3, participant characteristics reported; 4, intervention details reported; 5, principal confounders reported; 6, main findings reported; 7, variability in main outcomes reported; 8, adverse events reported; 9, loss to follow-up reported; 10, probability values reported; 11, source population representative of entire population; 12, study population representative of source population; 13, study setting representative of usual care; 14, participants blinded to intervention; 15, outcome assessors blinded; 16, no retrospective subgroup analysis; 17, analysis adjusts for different lengths of follow-up of participants; 18, statistical tests are appropriate; 19, reliable compliance with intervention; 20, outcome measures are valid and reliable; 21, recruitment of study groups from same population; 22, recruitment of participants over same period; 23, randomization of participants; 24, allocation concealment; 25, adjustment for confounding variables in main analysis; 26, adjustment for loss to follow-up in main analysis; 27, inclusion of sample size calculation.

Supplementary Material 4 table s5: Breakdown of patient and injury characteristics relevant to inclusion and exclusion criteria; across studies enrolling patients with mild TBI

|                                    | Inclusion criteria                                                                                                        |                              |     |                      |                                 | Exclusion criteria                                               |                |                                                                        |                            |                              |                             |                                    |                   |  |
|------------------------------------|---------------------------------------------------------------------------------------------------------------------------|------------------------------|-----|----------------------|---------------------------------|------------------------------------------------------------------|----------------|------------------------------------------------------------------------|----------------------------|------------------------------|-----------------------------|------------------------------------|-------------------|--|
|                                    | mTBI patient number at 3 months post injury, type and number of controls. Recruitment site(s)                             | age range in years           | MOI | LOC duration minutes | PTA duration hours              | (i)intoxicated at presentation or(ii) hx of drug and alcohol use | Hx of dementia | Hx of (i) psychiatric or (ii) neurologic illness or (iii) previous TBI | No CT scan performed in ED | CT shows intracranial injury | non native language speaker | Unable to consent /engage with FUP | DNA any follow up |  |
| Candrian et al <sup>19</sup>       | 35 patients reporting clinical impairments within 1 week after injury<br>35 matched healthy controls<br>4 Swiss hospitals | 17-64                        | Any | 0-30                 | PTA 0-1 Retrograde 0-30 minutes | +(i) and (ii)                                                    | +              | +(i,ii,iii)                                                            | -                          | +                            | -                           | +                                  | +                 |  |
| Carroll et al <sup>20</sup>        | 61 patients plus extracranial injury and healthy matched controls<br>Single English Major Trauma Centre                   | Any                          | Any | Any                  | Any                             | -                                                                | -              | +(i,ii,iii)                                                            | +                          | -                            | -                           | -                                  | +                 |  |
| Chakroun Walha et al <sup>21</sup> | 91 patients 2 Tunisian EDs                                                                                                | 18+                          | Any | Any                  | Any                             | -                                                                | -              | -                                                                      | -                          | +                            | -                           | +                                  | -                 |  |
| Chiang et al <sup>22</sup>         | 100 patients<br>Single Taiwanese neurosurgical outpatients                                                                | >19                          | Any | <30                  | 0-24                            | (ii)                                                             | +              | +(i,ii,iii)                                                            | -                          | -                            | -                           | -                                  | -                 |  |
| Heitger et al <sup>23,24,39</sup>  | 37 patients 37 healthy controls<br>Christchurch hospital New Zealand                                                      | 15-56                        | Any |                      | <24                             | (i) and (ii)                                                     | +              | (i),(ii) and (iii)                                                     | +                          | +                            | +                           | +                                  | +                 |  |
| Karaliute et al <sup>25</sup>      | 379 patients from single Norwegian Level 1 Trauma Centre                                                                  | 16-60                        | Any | <30                  | 0- 24                           | -                                                                | -              | -                                                                      | -                          | -                            | -                           | -                                  | -                 |  |
| Kraus et al <sup>26</sup>          | 1129 recruited from 2 Californian EDs plus non TBI injured controls with similar ISS                                      | 18-64                        | Any | <30                  | Any                             | -                                                                | -              | -                                                                      | -                          | -                            | -                           | -                                  | -                 |  |
| Madhok et al <sup>27</sup>         | 211 patients from 3 US Level 1 Trauma Centres                                                                             | >17                          | Any | Any                  | Any                             | -                                                                | -              | -                                                                      | +                          | +                            | -                           | -                                  | -                 |  |
| McMahon et al <sup>29</sup>        | 348 from 3 US Level 1 Trauma Centres                                                                                      | >17                          | Any | Any                  | Any                             | -                                                                | -              | (ii)                                                                   | +                          | -                            | -                           | -                                  | -                 |  |
| Nelson et al <sup>30</sup>         | 768-975 from 11 US Trauma Centres<br>240 Orthopaedic trauma controls                                                      | >17                          | Any | Any                  | Any                             | -                                                                | -              | (i),(ii)                                                               | +                          | -                            | -                           | -                                  | -                 |  |
| Richey et al <sup>31</sup>         | 2 John's Hopkins Emergency Departments in Baltimore US                                                                    | 240 aged <65<br>69 aged > 64 | Any | <30                  | <24                             | -                                                                | -              | -                                                                      | -                          | -                            | -                           | -                                  | -                 |  |
| Roe et al <sup>32</sup>            | 68 patients Admitted to Ullevål Neurosurgical Department within 48 hours of injury with ICD 10 S06.0-06.9                 | 16-60                        | any | any                  | any                             | -                                                                | -              | -                                                                      | -                          | -                            | -                           | -                                  | -                 |  |
| Sigurdadottir et al <sup>33</sup>  | 40 patients admitted to Ullevål University Hospital; CT within 24 hours of injury                                         | 16-55                        | any | any                  | any                             | (ii)                                                             | +              | (i), (ii)                                                              | +                          | -                            | +                           | -                                  | -                 |  |
| Thompson et al <sup>34</sup>       | 33 mild to moderate TBI within 24 hours of injury at Harbourview medical centre                                           | >20                          | any | any                  | any                             | +                                                                | +              | (ii),(iii)                                                             | -                          | -                            | -                           | -                                  | +                 |  |

Supplementary Material 4 table s5: Breakdown of patient and injury characteristics relevant to inclusion and exclusion criteria; across studies enrolling patients with mild TBI

|                               | Inclusion criteria                                                                                                                                              |                    |     |                      |                    | Exclusion criteria                                               |                |                                                                        |                      |                                |                             |                                    |                   |  |
|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----|----------------------|--------------------|------------------------------------------------------------------|----------------|------------------------------------------------------------------------|----------------------|--------------------------------|-----------------------------|------------------------------------|-------------------|--|
|                               | mTBI patient number at 3 months post injury, type and number of controls. Recruitment site(s)                                                                   | age range in years | MOI | LOC duration minutes | PTA duration hours | (i)intoxicated at presentation or(ii) hx of drug and alcohol use | Hx of dementia | Hx of (i) psychiatric or (ii) neurologic illness or (iii) previous TBI | No CT scan performed | Intracranial injury on CT scan | Not native language speaker | Unable to consent /engage with FUp | DNA any follow up |  |
| Verberne et al <sup>36</sup>  | ~ 182 Presenting to ED of 5 Netherlands hospitals and discharged alive to be enrolled at 6 weeks post injury                                                    | >18                | any | <30                  | <24                | -                                                                | -              | -                                                                      | -                    | -                              | +                           | +                                  | +                 |  |
| Vermeulen et al <sup>37</sup> | 1104 patients presenting within 24 hours of injury to EDs of 65 European Hospitals                                                                              | any                | any | any                  | any                | -                                                                | +              | (ii)                                                                   | +                    | -                              | -                           | -                                  | +                 |  |
| Yue et al <sup>38</sup>       | 260 patients presenting within 24 hours of injury to 3 US Level 1 Trauma Centres                                                                                | any                | any | any                  | any                | -                                                                | -              | (ii)                                                                   | +                    | -                              | +                           | -                                  | +                 |  |
| Machamer et al <sup>40</sup>  | 1480 presenting to 18 US Level 1 Trauma Centres within 24 hours of injury<br>219 Orthopaedic Trauma and 275 friend controls                                     | >17                | any | any                  | any                | -                                                                | -              | (i),(ii)                                                               | +                    | -                              | +                           | -                                  | -                 |  |
| Keatley et al <sup>41</sup>   | 253 patients from 2 John's Hopkins Emergency Departments in Baltimore USA                                                                                       | > 17               | Any | <30                  | <24                | -                                                                | +              | (i), (ii)                                                              | +                    | +                              | +                           | +                                  | -                 |  |
| Hume et al <sup>42</sup>      | 40 patients presenting to Alfred Hospital Melbourne<br>66 age matched trauma controls and 47 non trauma controls                                                | >= 65              | Any | <30                  | <24                | (i),(ii)                                                         | +              | (i)                                                                    | -                    | -                              | +                           | +                                  | -                 |  |
| Norrie et al <sup>43</sup>    | 263 presenting to Christchurch Hospital New Zealand                                                                                                             | Any                | any | <20                  | <24                | (ii)                                                             | +              | (i),(ii)                                                               | -                    | +                              | -                           | -                                  | -                 |  |
| Roy et al <sup>44</sup>       | 278 from recruited two EDs in Baltimore: Johns Hopkins Bayview Medical Center, a level-2 trauma center, and Johns Hopkins Hospital, a level-1 trauma center.    | >17                | any | <30                  | <24                | -                                                                | +              | (ii), (iii)                                                            | +                    | -                              | +                           | +                                  | -                 |  |
| Martha et al <sup>45</sup>    | 18 patients from single Level 1 trauma centre Seattle<br>CDC definition mTBI, adults- divided into age 21-54 and 55 and over 13 age matched uninjured controls. | >20                | any | <30                  | <24                | -                                                                | +              | (ii), (iii)                                                            | -                    | -                              | -                           | +                                  | +                 |  |
| Millier et al <sup>46</sup>   | 171 patients from single level 1 trauma centre                                                                                                                  | >17                | any | <30                  | <24                | -                                                                | -              | (i),(ii)                                                               | -                    | -                              | +                           | +                                  | -                 |  |
| Thuss et al <sup>47</sup>     | 154 patients with head injury with either LOC or amnesia presenting to single Dutch level 1 trauma centre                                                       | >59                | any | any                  | any                | (ii)                                                             | +              | (i),(ii),                                                              | -                    | -                              | +                           | +                                  | -                 |  |

Supplementary Material 4 table s5: Breakdown of patient and injury characteristics relevant to inclusion and exclusion criteria; across studies enrolling patients with mild TBI

#### Abbreviations and shading key

|                                                                                                                          |                                                                                      |                                                                                            |                                                              |                                                                            |                                                                                                             |
|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| mTBI = mild traumatic brain injury<br>MOI=mechanism of injury<br>LOC=loss of consciousness<br>PTA=post traumatic amnesia | Hx=history of<br>CT= Computed Tomography<br>Head Scan<br>US=United States of America | FUp=Followup<br>DNA=Did not attend<br>ED=Emergency Department<br>ISS=Injury Severity Score | =variable not relevant to<br>study inclusion or<br>exclusion | = variable cut off or sub category<br>defines study inclusion or exclusion | = study excluded any patient<br>with this variable or upper<br>and lower range specified<br>study inclusion |
|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|