

Open camera or QR reader and
scan code to access this article
and other resources online.



REVIEW

Clinical Assessment on Days 1–14 for the Characterization of Traumatic Brain Injury: Recommendations from the 2024 NINDS Traumatic Brain Injury Classification and Nomenclature Initiative Clinical/Symptoms Working Group

David K. Menon,^{1,*} Noah D. Silverberg,^{2–4} Adam R. Ferguson,^{5,6} Thomas J. Bayuk,⁷ Shubhayu Bhattacharyay,⁸ David L. Brody,⁹ Scott A. Cota,^{10,†} Ari Ercole,¹¹ Anthony Figaji,¹² Guoyi Gao,¹³ Christopher C. Giza,^{14,15} Fiona Lecky,¹⁶ Rebekah Mannix,¹⁷ Ana Mikolić,¹⁸ Kasey E. Moritz,¹⁹ Claudia S. Robertson,²⁰ Abel Torres-Espin,^{21,22} Spyridoula Tsetsou,²³ John K. Yue,²⁴ Hibah O. Awad,²⁵ Kristen Dams-O'Connor,^{26,27} Adele Doperalski,²⁸ Andrew I.R. Maas,^{29,30} Michael A. McCrea,³¹ Nsini Umoh,³² and Geoffrey T. Manley³³

¹Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK.

²Department of Psychology, University of British Columbia, Vancouver, British Columbia, Canada.

³Rehabilitation Research Program, Centre for Aging SMART, Vancouver Coastal Health Research Institute, Vancouver, British Columbia, Canada.

⁴Javad Mowafaghian Centre for Brain Health, University of British Columbia, Vancouver, British Columbia, Canada.

⁵Brain and Spinal Injury Center (BASIC), Department of Neurological Surgery, University of California San Francisco, San Francisco, California, USA.

⁶San Francisco Veterans Affairs Healthcare System, San Francisco, California, USA.

⁷Department of Neurology, Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA.

⁸Harvard Medical School, Boston, Massachusetts, USA.

⁹Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA.

¹⁰Former Branch Chief Traumatic Brain Injury Center of Excellence (TBICoE DHA), Biloxi, Mississippi, USA.

¹¹Division of Anaesthesia, University of Cambridge, Cambridge, UK.

¹²Paediatric Neurosurgery, Red Cross War Memorial Children's, Hospital Neurosciences Institute, University of Cape Town, Cape Town, South Africa.

¹³Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China.

¹⁴Departments of Pediatrics and Neurosurgery, UCLA Brain Injury Research Center, UCLA Mattel Children's Hospital, Los Angeles, California, USA.

¹⁵David Geffen School of Medicine at UCLA, Los Angeles, California, USA.

¹⁶School of Medicine and Population Health, University of Sheffield, Sheffield, UK.

¹⁷Division of Emergency Medicine, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA.

¹⁸Department of Psychology, University of British Columbia, Vancouver, British Columbia, Canada.

¹⁹Combat Casualty Care Research Program, US Army Medical Research and Development Command, Fort Detrick, Maryland, USA.

²⁰Department of Neurosurgery, Baylor College of Medicine, Houston, Texas, USA.

²¹School of Public Health Sciences, University of Waterloo, Waterloo, Ontario, Canada.

²²Department of Neurological Surgery, Brain and Spinal Injury Center, University of California San Francisco, San Francisco, California, USA.

²³Department of Neurology and Neurosurgery, Baylor College of Medicine, Houston, Texas, USA.

²⁴Weill Institute for Neurosciences, School of Medicine, University of California San Francisco, San Francisco, California, USA.

²⁵Division of Neuroscience, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, USA.

²⁶Department of Rehabilitation and Human Performance, Icahn School of Medicine, New York, New York, USA.

²⁷Department of Neurology, Icahn School of Medicine, Mount Sinai, New York, New York, USA.

²⁸Division of Neuroscience, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, USA.

²⁹Department of Neurosurgery, Antwerp University Hospital, Edegem, Belgium.

³⁰Department of Translational Neuroscience, Faculty of Medicine and Health Science, University of Antwerp, Antwerp, Belgium.

³¹Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, Wisconsin, USA.

³²Division of Neuroscience, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, USA.

³³Neurological Surgery, University of California San Francisco, San Francisco, California, USA.

[†]Current Chief Medical Officer-Primary Care, Biloxi VA, 400 Veterans Blvd, Biloxi, MS, USA.

*Address correspondence to: David K. Menon, MD, PhD, Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Box 93, Cambridge CB2 0NU, United Kingdom E-mail: dkm13@cam.ac.uk

Abstract

The current classification of traumatic brain injury (TBI) primarily uses the Glasgow Coma Scale (GCS) to categorize injuries as mild (GCS 13–15), moderate (GCS 9–12), or severe (GCS ≤ 8). However, this system is unsatisfactory, as it overlooks variations in injury severity, clinical needs, and prognosis. A recent report by the National Academies of Sciences, Engineering, and Medicine (USA) recommended updating the classification system, leading to a workshop in 2024 by the National Institute of Neurological Disorders and Stroke. This resulted in the development of a new clinical, biomarker, imaging, and modifier (CBI-M) framework, with input from six working groups, including the Clinical/Symptoms Working Group (CSWG). The CSWG included both clinical and non-clinical experts and was informed by individuals with lived experience of TBI and public consultation. The CSWG primarily focused on acute clinical assessment of TBI in hospital settings, with discussion and recommendations based on pragmatic expert reviews of literature. Key areas reviewed included: assessment of neurological status; performance-based assessment tools; age and frailty, pre-existing comorbidities, and prior medication; extracranial injuries; neuroworsening; early physiological insults; and physiological monitoring in critical care. This article reports their discussions and recommendations. The CSWG concluded that the GCS remains central to TBI characterization but must include detailed scoring of eye, verbal, and motor components, with identification of confounding factors and clear documentation of non-assessable components. Pupillary reactivity should be documented in all patients, but recorded separately from the GCS, rather than as an integrated GCS-Pupils score. At ceiling scores on the GCS (14/15), history of loss of consciousness (LoC) and the presence and duration of post-traumatic amnesia should be recorded using validated tools, and acute symptoms documented in patients with a GCS verbal score of 4/5 using standardized rating scales. Additional variables to consider for a more complete characterization of TBI include injury mechanism, acute physiological insults and seizures; and biopsychosocial-environmental factors (comorbidities, age, frailty, socioeconomic status, education, and employment). The CSWG recommended that, for a complete characterization of TBI, disease progression/resolution should be monitored over 14 days. While there was a good basis for the recommendations listed above, evidence for the use of other variables is still emerging. These include: detailed documentation of neurological deficits, vestibulo-oculomotor dysfunction, cognition, mental health symptoms, and (for hospitalized patients) data-driven integrated measures of physiological status and therapy intensity. These recommendations are based on expert consensus due to limited high-quality evidence. Further research is needed to validate and refine these guidelines, ensuring they can be effectively integrated into the CBI-M framework and clinical practice.

Keywords: CBI-M framework; classification and characterization; craniocerebral trauma; diagnostic techniques and procedures; Glasgow Coma Scale; NIH NINDS; pupil disorders; prognosis; traumatic brain injury

Introduction

This report from the Clinical/Symptoms Working Group (CSWG) of the 2024 National Institute of Neurological Disorders and Stroke (NINDS) TBI Classification and Nomenclature Workshop (hereafter referred to as the “Workshop”) provides a narrative expert review and pragmatic recommendations for the acute clinical characterization of patients with traumatic brain injury (TBI). We describe composition, processes, and findings of the Clinical/Symptoms Working Group. An overview of the new framework for the characterization of TBI and the NINDS TBI classification and nomenclature initiative is provided elsewhere.¹ In brief, the initiative is responsive to the National Academies of Sciences, Engineering, and Medicine (NASEM)’s 2022 consensus study report titled *Traumatic Brain Injury: A Roadmap for Accelerating Progress* (<https://nap.nationalacademies.org/login>

[.php?record_id=25394](https://nap.nationalacademies.org/login?record_id=25394)), which listed as its first recommendation: “Create and implement an updated classification system for TBI.” One of the aims of the initiative is to move from the conventional TBI severity classification of mild/moderate/severe in the acute phase based on a single assessment metric, to a richer classification characterized based on four pillars: clinical findings, biomarkers, imaging, and modifiers (a clinical, biomarker, imaging, and modifier [CBI-M] scheme). The present report from the CSWG should be viewed alongside those from the other five working groups involved in this initiative, and published in this special issue of the *Journal of Neurotrauma*. These include articles from working groups addressing: neuroimaging²; blood-based biomarkers³; psychosocial and environmental modifiers⁴; knowledge to practice⁵; and retrospective classification.⁶

The Glasgow Coma Scale (GCS)⁷ has been most widely used to clinically assess TBI severity. It was developed in 1974 as a standardized tool for assessing the level of consciousness after TBI but evolved into the gold-standard method for documenting and communicating overall TBI severity.⁸ Despite its well-known limitations for this purpose,⁹ it is enduring into its sixth decade. Traditionally, the total score is trichotomized into mild (GCS = 13–15), moderate (GCS = 9–12), or severe (GCS ≤8) classification.^{10–12} CSWG concluded that the GCS remains a very useful tool for TBI characterization; however, there is an opportunity to use it more effectively (e.g., report sub-scores and avoid trichotomization into mild/moderate/severe categories). The CSWG further concluded that supplemental clinical assessments are important, especially to characterize patients with GCS floor and ceiling scores.

The CSWG recognized that a wide range of assessment instruments and clinical findings other than the GCS have been used to document TBI severity. Two principles guided CSWG decision about which information to include and prioritize for implementation. First, the CSWG prioritized assessments that inform clinical decision-making in the acute care hospital setting, that is, those that drive triage, establish a diagnosis of TBI, optimize resuscitation targets to minimize secondary injury, trigger diagnostic interventions (such as blood biomarkers and neuroimaging), allocate patients to clinical pathways (discharge from the emergency department [ED], or admission to a hospital ward or intensive care unit [ICU]), and determine follow-up needs. Second, the CSWG prioritized assessments with prognostic import, harking back to the original goal of TBI severity classification.

The primary focus of the CSWG was clinical characterization of the severity of TBI, after TBI has been clinically diagnosed or suspected. There is an overlap between clinical assessment findings that indicate the presence of TBI and those that help grade its severity. For example, LoC immediately following head trauma is a sign that can rule-in a TBI diagnosis,^{13–15} while its presence and duration contribute to defining TBI severity. Although diagnosing TBI and then characterizing its severity is a logical sequence, following that order is not always possible. Diagnostic challenges often arise when it is difficult to confirm whether LoC and/or amnesia had actually occurred at the time of injury (classically in the following cohorts: patients with pre-injury cognitive impairment, young children), whether any amnesia that is documented is not conclusively attributable to TBI (such as in patients with pre-injury intoxication), and/or instances where a comprehensive assessment is impossible because of therapeutic interventions (such as sedation and tracheal intubation). In such cases, TBI may be “suspected”¹⁵

while injury characterization proceeds, such as with blood-based biomarkers and neuroimaging.

Methods

Working Group membership

CSWG consisted of 22 individuals (Supplementary Data) from five countries, including clinicians with expertise in adult, older adult, and pediatric populations, non-clinical researchers, and representatives of U.S. federal government agencies. The CSWG included members with a wide range of clinical and non-clinical expertise covering emergency medicine, neurosurgery, critical care, neurology, neuropsychology, and epidemiology. Our work was substantially informed and influenced by individuals with lived experience of TBI, public feedback, and discussions with other working groups before, during, and after the Workshop. In particular, their input highlighted the need for a more complete and nuanced characterization of TBI, rather than a crude classification as mild, moderate, and severe. We heard powerful testimony from these individuals about how such a crude classification could lead to “mild TBI” being dismissed as trivial (despite the common incidence of incomplete recovery at 6 months), while “severe TBI” might engender therapeutic nihilism and lose opportunities for good outcomes with aggressive management.

Of the 22 individuals in the CSWG, 18 substantive members were invited to participate, based on experience and expertise, through discussions with the Workshop Steering Committee (two of these were from low/middle-income countries, and three had specific experience in pediatric TBI). The remaining four members were early career researchers, who were initially inducted to the CSWG as Associate Members, but contributed substantially to the process and are recognized here as full authors of this article.

Scope

The scope of the work described in this article was decided by CSWG Chairs (D.K.M., N.D.S., A.R.F.) in discussion with the Workshop Steering Committee, and undertaken in the wider context of the NINDS TBI Classification and Nomenclature Workshop. We recognized that a large proportion of patients who sustain a TBI never present to the hospital. However, given the framework of the workshop, and given considerations of practicality, we agreed that the scope for our work would be limited to clinical assessment of TBI in patients presenting to the hospital.

Conventionally, the categorization of severity (and hence patient care and prognostic impressions) of TBI in the hospital setting has depended on initial assessment at presentation. However, TBI evolves over minutes, hours, days,¹⁶ and weeks.^{17–19} Therefore, it is not possible to fully assess the effects of TBI at a single early timepoint

(e.g., ED arrival),²⁰ and patients who initially look similar (e.g., GCS = 13 with subdural hematoma) may follow diverging trajectories after initial triaging assessment. Exploration of the full disease narrative of TBI was beyond the scope of our work. However, given this background, the CSWG aimed to cover assessment both at the point of hospital presentation (typically to an ED) and any evolution of clinical features over the first 14 days post-TBI, which informed diagnosis, triage, investigations, clinical interventions, and prognosis across the severity range in TBI. Trauma (and by extension TBI) is the leading cause of death for children in the United States (and many other parts of the world), but a detailed discussion of pediatric TBI was precluded by practical considerations regarding collation and analysis of further tranche of literature and article length. Consequently, while this article makes reference to pediatric TBI in several areas, the primary focus of this article is on adult TBI, and where appropriate, highlights issues pertaining to TBI in older adults.

Process

The CSWG met online on eight occasions (between June 2023 and January 2024) preceding the Workshop held at Bethesda, MD, on the 22nd and 23rd of January 2024. The work of the Working Group was informed by expert pragmatic reviews of the literature, led by one to three of the Working Group members with specific expertise on the topic, followed by detailed discussions of their evidence summaries in the Working Group meetings. Reviews covered the following topics:

- Clinical assessment of neurological status
- Performance-based assessment tools at the mild end of the severity spectrum
- Assessing and quantifying the impact of frailty, pre-existing comorbidity, and medication
- Characterizing extracranial injury and its impact on clinical care and prognosis
- Neuroworsening and discharge decisions for hospitalized patients
- Physiological monitoring in critical care
- Detection and quantification of physiological insults
- In addition, the CSWG prepared briefing notes outside this scope of work in specific areas where an evidence summary was thought to be useful and members or the CSWG had specific expertise, but these are not included in the current article. These were:
 - Clinical assessment of patients with TBI who do not present to the hospital; and
 - New approaches to data acquisition, management, and analysis

The outputs of this process were presented at (and informed by discussions at) Workshop Steering Committee

meetings (which included other Working Group Chairs) and a draft Summary Document was generated. This summary document was informed by discussions with members of the Knowledge to Practice Working Group, members of which attended one of our later Working Group meetings. Overlaps with other working groups (e.g., the “Modifiers” Working Group) were addressed through presentations of our plans at their meetings. The resulting modified Summary Document was circulated to the full membership of the other Working Group, and following feedback, a final Summary Document was placed online for public consultation on the Workshop Sharepoint. The recommendations in this document were presented at the Workshop in Bethesda, and informed by general discussion, and by the powerful personal testimony of the panel of individuals with lived experience of TBI. The Summary Document was further modified by a post-Workshop discussion of the CSWG in Bethesda, public feedback, subsequent online discussions of the Working Group, and discussions with the Workshop Steering Committee. These discussions led to a more detailed analysis of two areas—the possible integration of pupillary reactivity and GCS into a single score, and the use of single assessments of post-traumatic amnesia (PTA) as part of the acute assessment of TBI. These analyses were undertaken in large observational datasets and have been published elsewhere, but the results are summarized in our article. The current article is informed by this series of post-Workshop discussions.

Findings

Context

The CSWG recommends that any clinical assessment should be part of a comprehensive scheme that informs and is part of the characterization of TBI (Fig. 1). The clinical examination (C), along with blood biomarkers (B), and neuro-imaging (I) are three key pillars for description of TBI, and along with a consideration of modifying factors (M), provided an integrated CBI-M framework for characterizing TBI. The process undertaken by the CSWG resulted in a refinement of the focus of our discussion of the available evidence under the following headings: objective clinical examination of neurological status; mechanisms of injury; TBI symptoms; objective assessment of cognition, balance, and vestibulo-oculomotor dysfunction; extracranial injury; early physiological insults; age, comorbidities, and frailty; concurrent therapy; and dynamic assessments. Each of these is discussed separately below.

Objective clinical examination of neurological status. *The Glasgow Coma Scale Score.* The GCS is a highly pragmatic tool for documenting whether a patient has overtly normal alertness and clarity of

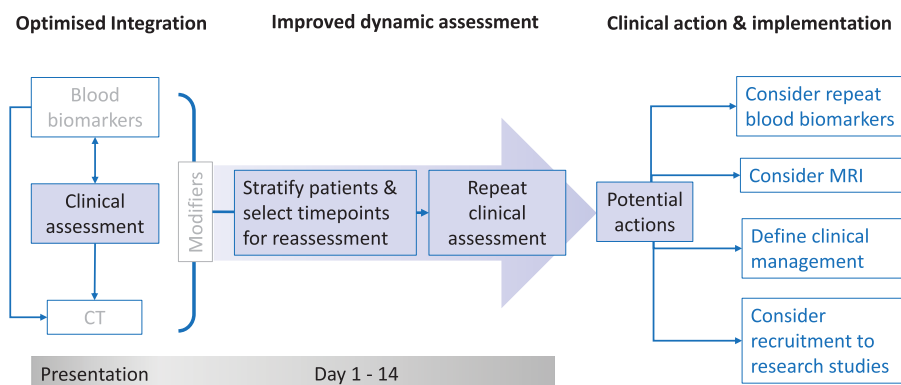


FIG. 1. Clinical assessment as part of clinical/biomarker/imaging-modifiers (CBI-M) assessment framework. Conceptually, initial clinical assessment would (in most cases) form the first step in a comprehensive characterization and inform need for repeat blood-based biomarker measurement and neuroimaging (including MRI), allocation to clinical care pathways, arrangements for follow-up, and prognostic expectations. This initial assessment would be enriched by a dynamic assessment of clinical progress over the first 2 weeks following TBI. Integration of information from such assessment would inform not just investigations and clinical care but also potential recruitment to research studies. We recognize that while other biofluids such as saliva and sweat may provide options for biomarker analysis in the future, we have primarily addressed the use of blood biomarkers in this scheme as those are closest to routine clinical practice. MRI, magnetic resonance imaging; TBI, traumatic brain injury.

thinking (GCS = 15), or presents with confusion (GCS = 14; GCS-V = 4, a core feature of “altered mental status”¹⁵), or reduced consciousness, including coma (GCS <9). However, the current use of the GCS, particularly in trichotomization of the total score (to “mild,” “moderate,” and “severe” TBI) has flaws. First, there is considerable variability in injury severity, treatment needs, and prognosis within each of the crude mild (13–15), moderate (9–12), and severe (≤ 8) categories. Information is better communicated by stating the actual GCS, ideally specifying subcomponent contributions, since these have different clinical and prognostic relevance. Second, the GCS has significant floor/ceiling properties, and imprecision is worst at extremes (sum scores of 3 and 15).²¹ Third, the application of the GCS requires modification in preverbal children²² and can be affected by pre-injury cognitive deficits.²³

It is critical to ensure that the procedures used to score the GCS follow standard approaches⁷ (see also <https://www.glasgowcomascale.org/> for details and instruction videos). Careful and consistent attention to detail is essential—for example, when the motor component is being scored, this is typically done in the upper extremities, with the response of the better arm recorded as the motor response.

Such conventional clinical assessment works to identify the need for CT brain imaging, early neurosurgery or critical care interventions, and appropriate post-ED clinical pathway selection. This approach reliably detects

neurosurgical lesions or pathology requiring other immediate attention.²⁴ However, most patients present with normal or minimally impaired consciousness and a “normal CT.” There is a common impression that a normal CT makes “clinically significant” TBI highly unlikely, and specific follow-up and rehabilitation is unnecessary. We now know that this view is unduly optimistic: many of this “mild” group who present to Level 1 Trauma Centers and meet thresholds for CT imaging suffer ongoing disabling symptoms.²⁵ Conversely, patients who present with a lower GCS may be subject to therapeutic nihilism and premature withdrawal of life-sustaining therapy (WLST),^{26,27} despite the fact that GCS assessment at presentation (particularly in patients with a sum GCS of 3) may be falsely lowered by alcohol, recreational drugs, sedative medication or tracheal intubation; or confounded by a post-ictal state or systemic physiological derangements (issues discussed in more detail in subsequent sections of this article). Further, a propensity-matched analysis suggests that a third of these patients might, with continued aggressive therapy, survive to independent recovery.²⁸ Additional assessment tools are needed to address these confounds.

Pupillary reactivity. Pupillary reactions to light provide a strong clinical biomarker that informs patient management and prognostication,²⁹ suggesting brainstem compression due to a space-occupying lesion or brain swelling, and while peripheral ocular or cranial nerve injury must be excluded, they have strong prognostic

import. It can be difficult to robustly diagnose the lack of pupillary reactivity to light by simple observation, especially when pupils are small, and automated pupillometry may provide a more consistent assessment.³⁰

It has been suggested³¹ that subtracting a point from the GCS for each unreactive pupil could generate an integrated “GCS-Pupils score (GCS-P)”. This provides a characterization of patients below a conventional GCS floor of 3, where patients lose an additional point for each unreactive pupil. Thus, patients with a conventional GCS score of 3 and one unreactive pupil would be scored as GCS-P = 2, and those with both unreactive pupils scored as GCS-P = 1. While conceptually appealing, there are both statistical disadvantages and practical difficulties with this approach:³²

- The prognostic information provided by the GCS-P score is greater than the sum GCS on its own, but this increment is only about half of that provided by including the pupillary responses as separate variables (Supplementary Fig. S1)
- At a GCS ≥ 3 , a summary GCS-P score is necessarily ambiguous about whether points are lost for pupils or another GCS components (Supplementary Fig. S2)—and this ambiguity affects both likely prognosis and clinical decision-making.

This discussion leads us to strongly recommend assessing and recording pupillary responses to light, using automated pupillometry if possible, but record these separately from the GCS, rather than as a combined GCS-P score.

Timing and confounding factors. These clinical assessments may vary significantly in the immediate post-injury period (either improvement after the initial ictus or clinical deterioration (“neuroworsening”; see later), which makes them subject to substantial variability depending on when they are measured. Furthermore, early data from the pre-hospital setting may rely on first responders, in which context assessment levels of consciousness may be less reliable and reproducible. Thus, reliable data are often missing early in the patient’s course. The best initial GCS might reasonably be expected to most faithfully capture the severity of the initial injury. However, it may also be confounded by hypoxia or hypotension, but the concept of “best resuscitated” GCS is not relevant to modern pre-hospital practice where resuscitation and stabilization may all occur concurrently and frequently require sedation and endotracheal intubation. Therefore, while later assessments of GCS by more experienced practitioners might be expected to be more complete, for the more severely injured patients, these might not be fully assessable as these patients would likely be intubated, sedated, paralyzed, and mechanically ventilated.

We are, therefore, faced with how to best use GCS/pupillary responses assessed at a variety of timepoints, many of which might be missing. Imputation strategies have been examined using data from the CENTER-TBI dataset.³³ Where we need to choose a “most predictive” neurological assessment from variably missing data, a substitution strategy is needed but there are a variety of possible choices as to which GCS/pupillary assessment to choose. Model performance (in terms of pseudo-R² explained “pseudovariance”) varies somewhat with both substitution strategy and type of model (e.g., dichotomous vs. ordinal regression) and so the choice is not an entirely trivial one.

One approach to the confound of tracheal intubation has been to limit assessment to the motor subscore (which is strongly prognostic in patients with GCS 3–12).³⁴ However, in the overall TBI population, the GCS sum performs better than the motor score alone overall, so there is a case for exploring alternative strategies.³⁵ Of a variety of choices, the strategy used by the International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT)³⁴ generally works well and is simple: the ED discharge assessment GCS/pupil assessment is used. If this is missing, this is substituted with an alternative available value, moving backwards in the patient’s clinical course (i.e., ED discharge → study hospital ED arrival → referring hospital ED arrival → pre-hospital).³³

One uncertainty is that pupillary responses may remain assessable even when the GCS is not, and this could lead to discordances in the time of recording. For example, a patient with an expanding extradural hematoma may have had a well-documented GCS of 15 at the scene of the injury, but subsequently show neuroworsening, develop an unreactive pupil, and require sedation and tracheal intubation. In this context, the GCS is un-assessable due to sedation and a sedation hold is inappropriate. In these circumstances, it would seem inappropriate to combine the most robustly documented GCS (of 15) with report of an unreactive pupil. The CSWG concluded that it might be best to record the last GCS before intubation, which integrates the effect of neuroworsening.

Where a GCS component is untestable, several options are available, but the amount of detail that can be obtained is always constrained by the burden of data recording. In the past, un-assessed motor and verbal scores were as 1—but this is not optimal.³³ An alternative,⁷ which we would recommend, is not to score it as 1, but rather to specify this, and amend notation to this effect. For example, in the past, the notation of “V(t)” has been used in an intubated patient. However, there may be other constraints to full GCS assessment, and if a complex notation system is to be avoided, perhaps all untestable components could be specified with a single notation (“U”: e.g., V(U)), which in subsequent group level

research analyses could mark scores for imputation. However, such usage (on its own) makes calculation of a sum GCS impossible (since there is no score attached to an untestable component). A compromise would be to score the untestable component as “1” for calculation of a sum score, and append the “U” as a suffix (e.g., GCS 3U, broken down as E(U) V(U) M(U) for a sedated and intubated patient).

Less binary confounds (e.g., sedation, a recent seizure) may allow some scoring, and it is not clear what the best approach should be. In research settings, well-justified imputation may be the best option. However, it remains unclear which of these strategies is optimal, and the best options may vary depending on whether the goal is individual TBI characterization in clinical practice, or analysis of a research dataset.

Alternatives to the GCS. Alternative severity classification and diagnostic schemes (e.g., FOUR Score,³⁶) are not optimal approaches for characterizing TBI across the severity spectrum in the acute phase. Similarly, while the presence or absence of LoC is often recorded, there is inconsistent evidence that this binary variable provides prognostic information, so the CSWG would not recommend it in isolation.^{37,38} The Alert, responds to Voice, responds to Pain, Unresponsive (AVPU) scale is commonly used in pre-hospital and emergency care and provides a more nuanced, but still unitary measure of consciousness. While the AVPU score does correlate with the GCS, very few studies have examined its use in early TBI assessment.³⁹

Detailed neurological examination. Detailed evaluation of neurological function (e.g., lateralizing weakness, language deficits, ocular dysfunction, cerebellar signs) is recommended as part of a comprehensive clinical examination,⁴⁰ and ongoing neurological monitoring can inform diagnosis and management decisions (see “*neuroworsening*,” later). However, these assessments are not systematically and consistently performed or documented in the acute care setting in the ED. It is very likely that at least some of these assessments are important in the early characterization of TBI, but the systematic incorporation of these assessments into clinical care, and recommending the best format for recording their findings, will require further evaluation of their sensitivity, specificity, reliability, and robustness in the ED setting.

Post-traumatic amnesia

The duration of post-traumatic amnesia (PTA), especially in the range of 1–60 days, is highly prognostic when assessed prospectively with validated tools,⁴¹ such as the Galveston Orientation and Amnesia Test (GOAT), Westmead PTA Scale, or O-Log. A study directly comparing these three instruments found that the Westmead PTA Scale took the longest to normalize after TBI, whereas patients who passed the other PTA tests often had

ongoing agitation and memory impairment, suggesting persisting PTA.⁴² The international INCOG expert group recommended the Westmead scale for PTA assessment.⁴¹

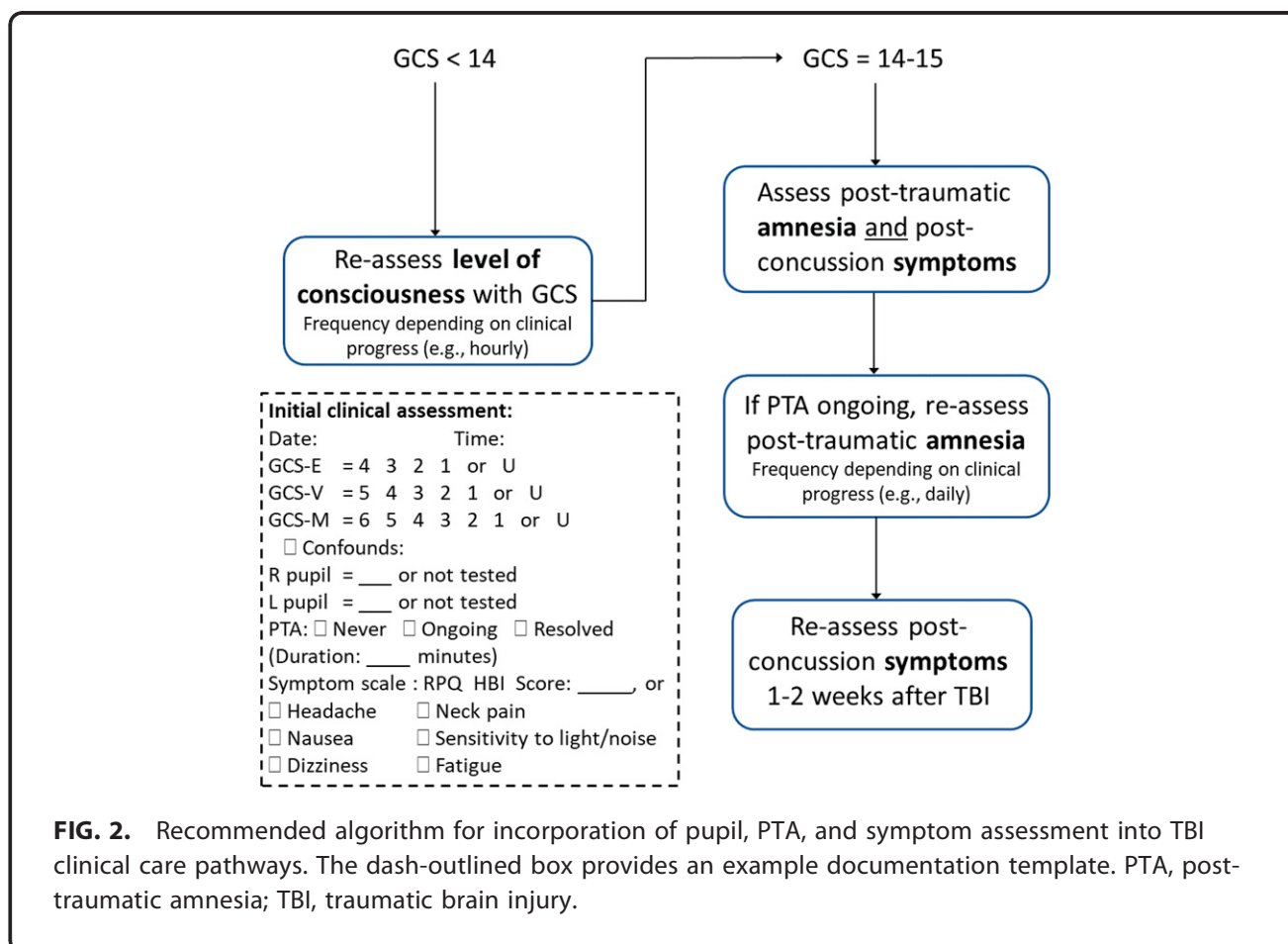
Initial assessment of PTA is not always necessary or feasible in the emergency setting. Patients with clear evidence of confusion or impaired consciousness need not be assessed with a PTA scale (see Fig. 2), but rather only those with GCS = 15 or GCS = 14 where documentation of confused behavior is absent or equivocal. Feasibility issues include insufficient time and prominent confounding factors, e.g., opiate analgesic medications can impair episodic memory and lower performance in the Westmead PTA Scale.^{43,44}

Finding that a patient has ongoing PTA in the ED may have implications for clinical decision-making, such as whether to order a head CT,⁴⁵ move the patient to a secure and low-stimulation environment,⁴¹ or discharge them home with supervision or admit to hospital for observation.²⁴ If a patient is still in PTA (or coma), serial PTA testing after transfer from the ED will be necessary to accurately monitor emergence from PTA and quantify its duration.⁴¹ Prospective serial assessment is important because retrospective estimation of PTA months after the injury is unreliable.⁴⁶ That said, it may be more useful than no information about PTA.

Many patients will have experienced a period of PTA that resolved prior to their arrival at the ED. If a patient is confirmed to not be in PTA on ED assessment, the clinician should query for resolved PTA by asking the patient if they remember the impact and moments after, what their first memory following the impact is, and when their memories became continuous again, suggesting emergence from PTA. Subtracting the time of emergence from PTA from time of injury can provide a crude estimate of PTA duration. A crude estimate may be sufficient in this context because although PTA duration in the range for 1–60 days is highly prognostic, PTA duration within the range of 0–24 h appears less so.^{37,38} Another rationale for querying pre-hospital arrival PTA is that can help rule-in a diagnosis of TBI in a patient without other acute signs.¹⁵

In summary, the CSWG recommend that patients with a GCS of 14–15 should have the presence of PTA assessed and the resulting information be incorporated into clinical care pathways as suggested in Figure 2.

Mechanisms of injury. Low energy transfer mechanisms (e.g., falls from a standing height or <2 m in adults) are conventionally expected to result in less severe injury than high-velocity injury (e.g., road traffic collisions, falls from a greater height), and information on injury mechanisms should be routinely recorded.²⁴ However, even low energy transfer incidents (especially falls in infants and older patients) can cause significant



injury that is under-estimated by conventional clinical assessment, results in under-triage and inadequate or delayed investigation or treatment.⁴⁷ Assessment of the mechanism of injury is usefully supplemented by data regarding protective measures (seat belts, airbags, helmets) that might mitigate the injury, since these can substantially reduce the extent of injury.⁴⁸

TBI symptoms. Traditional indicators of neurological status such as GCS exhibit minimal variability and ceiling effects, and have limited utility in the large proportion of patients with TBI who present with a GCS of 15, have emerged from PTA, and have a normal CT. Prospective cohort studies in non-hospitalized TBI have considered a broader range of clinical variables available in the ED and found that most have limited prognostic value.^{38,49–51} ED assessment of symptoms (e.g., headache, dizziness, sensitivity to noise) using validated scales may be an exception, with some evidence in both children^{52,53} and adults,^{51,54,55} for age-appropriate scales. Relevant instruments include the Rivermead Post Concussion Symptoms Questionnaire for adults; and the Health Behavior Inventory (the symptom scale embedded in the Child Sport Concussion Assessment Tool 6) for children. There is also more robust evidence for the prognostic utility of acute symptom assessment

following sport-related concussion,⁵⁶ which could be reasonably extrapolated. The evidence that symptoms are prognostic primarily applies to patients with a GCS of 15 (or a verbal score of 5)—but it is reasonable to record symptoms in patients with a GCS verbal score of 4. The evidence for presence/absence of specific symptoms in ED is mixed.^{51,52,54,55,57} Symptom severity ratings may be more prognostic than symptom presence/absence,⁵⁸ perhaps because they contain more granular information and have more variability. Symptom reporting in the 7–14 days following injury has been consistently shown to improve prognostic accuracy in non-hospitalized TBI over and above demographic and clinical variables,^{37,50,51,54} and acute symptoms measured in the ED.^{58,59} For this reason, the clinical assessment algorithm (Fig. 2) recommends both acute and follow-up symptom assessments. More broadly, the variable prognostic utility of symptoms provides a strong argument for integrating bio-fluid biomarker and neuroimaging data into a comprehensive assessment of TBI.

Studies that evaluate the prognostic utility of post-concussion symptoms are summarized in Supplementary Table S1a and b. These studies used varied symptom lists, administration modalities (e.g., interview vs. self-report), response options, and scoring methods (e.g.,

symptom count vs. summed item severity ratings), between 0 and 20 days following injury. Few of these studies included pediatric patients, and there is almost no literature relevant to the relationship of symptoms and outcomes in children <5 years of age. All studies reported strong associations with outcome, as measured by the Glasgow Outcome Scale-Extended or the presence of multiple persistent symptoms at 1–6 months follow-up.

Objective assessment of cognition, balance, and vestibulo-oculomotor dysfunction. There is emerging evidence that assessing cognition with standardized objective tests in the ED or soon after may further refine the prognosis of non-hospitalized TBI.^{60–66} CSWG found inadequate evidence to support the prognostic utility of performance-based clinical assessment tools after non-hospitalized TBI. Standardized objective tests of cognition have been most studied for prognostic utility. They have demonstrated significant associations with outcome in multiple studies.^{60–67} However, most studies used different cognitive tests and involved small samples, without confound adjustment or external validation. Because objective cognitive tests have prognostic utility in hospitalized TBI,^{68–70} they have the potential to contribute to the classification of TBI across the severity spectrum. Other performance-based clinical assessment tools such as the King-Devick Test,^{71–73} Vestibular/Oculomotor Screening Test,^{73–77} Buffalo Concussion Treadmill Test,^{78,79} EyeBox,⁸⁰ and various measures of standing balance or gait^{81–83} have been explored for their prognostic utility in various settings but their relative prognostic utility at different time points after injury has not been established. Moreover, findings from these studies are inconsistent and may not be representative as they are almost exclusively based on studies with athletes who sustained a sport-related concussion, a narrow segment of the non-hospitalized TBI population. Importantly, it is as yet unclear if any performance-based clinical assessment tools can predict outcome over and above symptom severity ratings, which are more feasibly obtained.

Additional clinical evaluations for specific populations

In specific populations, additional clinical evaluations should be considered. For example, the U.S. Department of Defense recommends the use of the Military Acute Concussion Evaluation version 2 (MACE 2) in service members with suspected TBI, GCS 13–15, and no “red flags” concerning more serious injury (<https://health.mil/Reference-Center/Publications/2020/07/30/Military-Acute-Concussion-Evaluation-MACE-2>). The MACE 2 includes a brief, standardized neurological examination that can be

performed consistently by providers with a wide range of training and experience (PMID: 32808563). It also includes the Vestibulo/Ocular-Motor Screening (VOMS) recommended for those who are not overtly symptomatic at baseline and do not have unstable cervical spine. The VOMS consists of a series of provocative maneuvers that may bring out otherwise occult concussion-related symptoms.⁸⁴ The scores on the MACE 2 including symptoms provoked by VOMS can be tracked serially over time to measure recovery, guide progressive return to activity, and assist with return-to-duty decision-making (<https://health.mil/Reference-Center/Publications/2024/02/23/Progressive-Return-to-Activity-Primary-Care-for-Acute-Concussion-Management>). However, evidence for the longer-term prognostic utility of the MACE 2 is inconsistent at present.^{59,85}

Extracranial injury. Compared with isolated TBI, polytrauma is associated with a higher risk of moderate disability and severe disability/death, at both 3 and 6 months.^{86,87} These worse outcomes may be due to the injury itself, a higher risk of early hypoxia and hypotension,⁸⁸ an aggravated detrimental host response,⁸⁹ and/or the effects of anesthesia and surgery needed for extracranial injuries.⁹⁰ These considerations mandate a systems-based tertiary trauma assessment in all patients with TBI. A range of trauma severity assessment tools have been used in this context, but the Abbreviated Injury Score (AIS)⁹¹ is probably most widely used. Both the head AIS and the Injury Severity Score (the sum squares of AIS scores in the three most severely injured regions) may be of some prognostic value in TBI,⁹² but an AIS ≥ 3 in any individual extracranial region also provides a convenient and pragmatic threshold for identifying extracranial injuries that are of relevance in the integrated characterization of multiple trauma that includes TBI, in registries and research studies.⁸⁶ If a formal assessment of AIS is thought to be less practicable for routine clinical evaluation, a useful approximation may be to record any injury that would, in isolation, have required hospital admission.^{86,87} Characterization of the severity of extracranial injuries is included in the Modifier Pillar of the CBI-M model. Such an integrated assessment of the severity of TBI and extracranial injury provides the best basis to plan extracranial surgery (balancing the risks and benefits of early definitive treatment against the risks of perioperative physiological compromise in a vulnerable brain). Such an assessment also allows for rational planning of follow-up and rehabilitation.

Early physiological insults and seizures. Hypoxia, hypotension, hypothermia, and fever at presentation have all been associated with worse outcomes in TBI, and their presence should be recorded in any complete clinical characterization of TBI. However, the most appropriate

thresholds for identifying these insults are still not clear and the field is still evolving. For example, Traumatic Coma Data Bank (TCDB) data suggested a systolic blood pressure (SBP) threshold of 90 mmHg,⁹³ but more recent publications suggest a higher thresholds,⁹⁴ or a U-shaped association with outcome⁹⁵ Similarly, while TCDB data focused on hypoxia,⁶⁰ there is increasing exploration of hyperoxia as a risk factor,⁹⁶ and early (spontaneously achieved) peak temperatures below 37°C or above 39°C are associated with worse outcomes.⁹⁷ Despite these epidemiological associations, precise thresholds for defining harmful levels of blood pressure, oxygen saturation, and temperature remain unclear, as do the indications and means for treating these. Consensus-based thresholds (such as those identified by the American College of Surgeons Trauma Quality Improvement Program Guidelines⁹⁸) may be useful to define hypoxia and hyperoxia, hypotension and hypertension, and hypothermia and fever, until definitive data emerge on this. While not discussed here, it is also important to recognize that blood pressure norms (and by extension, harm thresholds and clinical targets) vary substantially with age,^{99–102} a consideration that is critical in managing pediatric TBI. While hypoglycaemia, hyperglycaemia, and hyponatremia represent additional important metabolic insults⁹⁸ and are often available at the time of ED assessment in patients, they are not part of clinical assessment, and are hence not covered here.

Early post-traumatic seizures have been independently associated with increased need for ICU admission, longer hospital stay, dependency at discharge, and worse functional outcome.¹⁰³ It is important to record the presence of early post-traumatic seizures not only because of these associations but also because a post-ictal state may be responsible for impairment of consciousness, and provide a reason for caution against estimating TBI severity simply based on the GCS.

Age, comorbidities, and frailty. Age is among the strongest outcome predictors in TBI, with mortality and unfavorable outcome increasing continuously with age through adulthood.^{104,105} This may be due to reduced physical or neurological reserve, and/or the presence of comorbid disease, which is often (though not exclusively) associated with aging. The exception of these trends is in children, where infants have a higher mortality rate than older children,¹⁰⁶ and other outcomes have complex relationships with age.¹⁰⁷ While such knowledge should inform how clinicians counsel patients and families about prognosis and the benefits of aggressive therapy, it is important to avoid a nihilistic response to TBI management in all older patients, since such nihilism may (in itself) contribute to inconsistent WLST^{25,26} and poor outcomes.¹⁰⁸ Indeed, even in an ICU setting, a significant proportion of such older patients may achieve a favorable recovery with appropriate

therapy.¹⁰⁹ More refined approaches are needed to assess the impact of age and pre-existing disease.

One key approach is to refine age-related vulnerability by recording frailty, a term used in both adults and children, which quantifies loss of physiological and cognitive reserve, and may increase vulnerability to the stress of trauma. Additional Frailty scales may be based on the presence of comorbidities (such as the Charlson Comorbidity Index [CCI], which can be reliably abstracted from electronic patient records¹¹⁰; the 70-item Canadian Study of Health and Aging [CSHA] Frailty Index¹¹¹; the modified 5- and 11-item Frailty Index [mFI-5 and mFI-11]¹¹²; and a five-item Pediatric Frailty Scale).¹¹³ The mFI-5 and mFI-11 are associated with worse outcome in TBI,^{114,115} and a novel 30-item scale was also associated with worse TBI outcome in the CENTER-TBI and TRACK-TBI studies.¹¹⁶ While these scales clearly have research relevance, they may be difficult to implement in practice. Global clinical assessments, such as the CSHA Clinical Frailty Scale (CFS),¹¹¹ associate with the outcome, with threshold scores of ≥ 4 ¹¹⁷ or ≥ 3 ¹¹⁸ on the 9-point CFS associated with a ~ 90 – 95% risk of death or severe disability. The CFS may provide a more pragmatic option for recording frailty in the context of clinical TBI management.

The discussion above primarily focuses on physical comorbidities and systemic physiological reserve, both of which have been shown to be important in modulating TBI outcome.¹¹⁹ These scales also address pre-injury neurological status but only in the context of established diagnoses. Current assessments do not address cognitive reserve or psychological health—both of which can be critical determinants of TBI outcome (and are covered by another Working Group). There is a need for better means of quantifying the impact of these factors.

Other considerations apply at the younger end of the age spectrum. In young children, early recovery may be excellent, but children who sustain a TBI and appear to recover fully may be on a different developmental trajectory from their uninjured peers, and disabilities may only manifest years after the injury.¹²⁰ It is unclear whether initial assessment tools can identify children most at risk of such adverse late outcomes, and research in this area is needed.

A separate article in this series⁴ provides further consideration of Psychosocial and Environmental “Modifiers” that can impact outcome (independent of injury severity) or influence assessment.

Concurrent therapy. It is critical that a full characterization of acute TBI also records pre-injury therapies that the patient is receiving, with particular attention to medication that may affect the disease course in TBI. While several drugs may be relevant in this context, anticoagulants and antiplatelet agents have a direct impact on

hematoma expansion and outcome, and are most widely addressed in the literature.¹²¹

Additional information over the first 2 weeks post-injury. TBI pathophysiology evolves over time, and incorporating additional clinical information over the initial course provides an improved selection of patients for acute therapy and follow-up and refines late (months to years) prognostication. The ways in which such dynamic information is collected will depend on TBI severity and care path.

For non-hospitalized TBI. Assessing post-TBI symptom severity (using the Rivermead Post Concussion Symptoms questionnaire or comparable instruments) up to 14 days after injury has been repeatedly shown to refine prognosis,^{37,51,54} likely above and beyond acute symptom severity. Several studies additionally measured mental health symptoms using validated self-report scales, designed to quantify symptoms of depression (e.g., PHQ-9),¹²² anxiety (e.g., GAD-7),¹²³ and/or post-traumatic stress (e.g., PCL-5),¹²⁴ and found that these scales explained unique variance in outcome from non-hospitalized TBI.^{55,57,125} Symptom assessment could also inform the need for repeat biomarkers, further follow-up, MRI, or inclusion in trials (Fig. 1). For logistic reasons, attempts have been made to identify, at presentation, patients particularly high risk of persistent symptoms for such follow-up,⁵¹ but this remains an imperfect process, and an area in which future research should be prioritized.

For hospitalized TBI, ongoing assessment of neurological status, intracranial and systemic physiology, and therapy requirements provides important information for characterizing TBI and informing prognostication. Specific items include:

- Clinical neuroworsening (drop in GCS, seizures, progression of neurological deficit, development of a new neurological deficit, or new pupillary abnormality) is important for both prognosis and therapy.¹²⁶
- Monitoring of systemic physiology, intracranial pressure, brain oxygenation and metabolism, and electrophysiology (which may allow detection of non-convulsive seizures); and charting of therapy intensity level and response.^{127,128} It is likely that, in the future, these complex data can be usefully integrated and synthesized using novel data science approaches (including machine learning and artificial intelligence) to provide decision support tools that allow more individualized and precise management and prognostication. These can either cover the entire disease narrative of TBI for general prognosis of outcomes,^{129–131} or address more specific contexts, such as prediction of intracranial hypertension,^{132–134} emergence from coma,¹³⁵ and predicting benefit from rehabilitation.¹³⁶ However, the clinical use of such

tools is still being developed, and no validated applications are currently available. Consequently, this is best considered an important area for research, rather than a recommendation for routine clinical use.

- Daily assessment of post-traumatic amnesia, using the GOAT, Westmead Post Traumatic Amnesia (WPTA) Scale, or O-Log⁴¹ in the period of emergence following hospitalized TBI can improve prognostication over and above the initial GCS score.^{137–139}

Conclusions

The CSWG assessed the features available for characterization of patients following TBI based on their value in informing prognostication and informing clinical decision-making and clinical care in the acute care hospital setting. Key targets included appropriate triage, accurate diagnosis of TBI, optimized resuscitation targets to minimize secondary injury, triggers for diagnostic interventions (such as blood biomarkers and neuroimaging), allocation of patients to clinical pathways, and identification of follow-up needs. The recommendations of the CSWG are summarized in Table 1.

The CSWG concluded that the GCS continues to provide an excellent clinical basis for TBI characterization of patients with TBI. However, current trichotomized categorization of TBI as mild/moderate/severe is not fit for purpose, and can lead to imprecise prognostication and inappropriate clinical management.

Appropriate use of the GCS requires recording of the full GCS sum score (ideally post-resuscitation), with breakdown of its eye, verbal, and motor components to allow appropriate characterization of patients. There needs to be explicit identification of confounds to assessment (e.g., alcohol or drug effects) and untestable components (as “U”; e.g., due to endotracheal intubation). However, the optimal approaches to assessing and recording GCS in such settings need further work. All patients should have pupillary reactivity to light in both eyes assessed and recorded separately from the GCS. The GCS has ceiling and floor effects, and in patients with a sum GCS score of 14/15, the Working Group recommended recording a history of LoC and the presence and duration of post-traumatic amnesia (PTA) using validated tools. In patients with a verbal GCS score ≥ 4 , acute symptoms should be documented, using standardized rating scales appropriate for the context of use.

Other key variables include injury factors (mechanism, injury velocity, and impact mitigation factors) and acute physiological insults (based on expert consensus thresholds). A more complete characterization of TBI should also include biopsychosocial-ecological vulnerabilities: comorbidities, concurrent therapies, assessment of frailty in addition to age (using validated instruments),

Table 1. Recommendations of the Clinical/Symptoms Working Group: Clinical Characterization of TBI <24 h Post-Injury^a**(1) Basic clinical descriptors**

For all patients, the following must be recorded:

Glasgow Coma Scale (GCS) (full breakdown: motor (M), verbal (V), and eye (E) components).

- Use post-resuscitation GCS for consistency.
- Explicitly note confounds (e.g., intoxication, sedation, intubation).
- Untestable GCS components should be marked with the suffix “U” (untestable) and scored as 1 in sum GCS^b

Pupillary responses:

- Report independently from GCS, but assess at the same time as GCS.
- Avoid using an integrated GCS-P score.
- Use automated pupillometry when possible.

(2) Expanded clinical characterization

For a more complete TBI assessment, record:

Injury factors:

- Mechanism, impact velocity, and mitigation (e.g., seat belts, airbags, helmets).
- Extracranial injuries that would warrant hospital admission, even in the absence of a TBI
- Early physiological insults (to include hypoxia and hypotension; based on TQIP consensus thresholds)
- History of loss of consciousness (LoC)
- Presence and duration of post-traumatic amnesia (PTA) duration, ideally determined by prospective serial assessment with a validated tool.
- Record assessment point (e.g., arrival to trauma ward) and time post-injury
- In patients with GCS verbal score >4 in ED: document acute symptoms, ideally with standardized rating scales

Biopsychosocial-ecological vulnerabilities:

- Physical/psychological comorbidities.
- Relevant therapies (especially those affecting hemostasis).
- Age, frailty, socioeconomic status, education, and employment status.

Dynamic assessment:

- Record neuroworsening (GCS, pupillary reactivity, neurological examination) over the first 7–14 days.
- Monitor symptom severity over first 7–14 days in patients not admitted to the hospital.

(3) Emerging clinical variables

Consider these additional assessments, though further validation is needed of their use and utility:

- Vestibulo-oculomotor dysfunction and balance, particularly for less severe cases.
- Cognitive assessment: standardized objective tests soon after injury (no specific platform recommended).
- Mental health: assess symptoms 7–14 days post-injury using validated scales.

Research recommendations

- Address empirical validation, refinement, implementation, and impact of the recommendations listed above.
- Define optimal approaches for assessment and notation where components of the GCS are not assessable
- Define the objective and widely accepted thresholds to characterize the full range of physiological insults.
- Evaluate data-driven tools that integrate dynamic and imputed data for prognostication and decision support.

^aThese recommendations apply to patients presenting to hospital <24 h post-injury, with features recorded as part of a clinical, biomarker, imaging (CBI) framework, as well as recording modifiers (M) that may affect assessment or modify expected outcomes. Items in the clinical (C) pillar of CBI-M are classified into three categories, with a separate listing of research recommendations.

^bUntestable: e.g., M_U V_U E_U = GCS: 3U for a patient who is sedated and intubated.

TBI, traumatic brain injury; TQIP, trauma quality improvement program.

socioeconomic status, educational attainment, and employment status. Finally, the CSWG recognized the importance of recording disease progression or resolution over the first 14 days—including neuroworsening in hospitalized patients, and serial assessment of symptom severity in all patients.

Additional assessments that have emerging (but as yet inconclusive) evidence for use include a detailed assessment of neurological deficits, vestibulo-oculomotor dysfunction, cognition (using standardized tests), and assessment of mental health symptoms. Data-driven integration of physiological status and therapy intensity could, in the future, provide decision support tools in hospitalized patients, but these require further refinement, validation, and implementation.

This article provides recommendations for clinical assessments as part of an integrated CBI-M scheme for patient assessment. Routine assessment of these clinical features, alongside blood-biased biomarkers, neuroimaging, and psychosocial/environmental modifiers, can refine TBI characterization and potentially improve injury

outcomes. However, it is critical to recognize that high-quality evidence for the use of the variables addressed in this article is limited. Consequently, these recommendations are based on expert consensus. Additional research is needed to validate the use of these recommendations, both individually, and as part of an integrated CBI-M scheme. Such research must address performance of the scheme in achieving better prognostic precision, and in improving clinical decision-making and care. However, it is also critically important that such evaluation also addresses issues in appropriate implementation of these recommendations, so as to establish robust links between knowledge and practice.

Acknowledgments

The authors are grateful to the National Institute of Neurological Disorders and Stroke (NINDS) for support and sponsorship of the 2024 NINDS TBI Classification and Nomenclature Workshop. The authors would like to thank Dr. Matthew Breiding (Centers for Disease Control and

Prevention, USA), Todd Cesar (Traumatic Brain Injury Center of Excellence, Defense Health Agency), Dr. Thomas Shanahan (Central Manchester NHS Trust), and Dr. Gordon Fuller (University of Sheffield) for providing input to discussions. The authors are very grateful for feedback received from the Workshop's steering committee, other working group members, and attendees, which provided important direction for this article. In particular, the authors are hugely grateful for the narratives provided by individuals with lived experience of traumatic brain injury—their experiences have provided unique insights that have informed our work. The authors also like to acknowledge organizational and administrative support for our meetings, provided by Infinity Conference Group & Rose Li and Associates.

Authors' Contributions

The report that underpinned this article was based on discussions within the Clinical Assessment Working Group. This report was refined through wide discussions at the NIH 2024 TBI Classification and Nomenclature Workshop, including valuable input from individuals with lived experience of TBI and public feedback. The article was drafted by D.K.M. with substantial input from N.D.S. and A.R.F., reviewed and revised by the Working Group members, and finalized by D.K.M., N.D.S., and A.R.F. with help from A.T.-E.

Disclaimer

The views expressed in this article are those of its authors, and the content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Neurological Disorders and Stroke or the National Institutes of Health and the U.S. Department of Health and Human Services.

Authors Disclosure Statement

D.K.M. was supported by the National Institute for Health and Care Research (NIHR, UK) through the Cambridge NIHR Biomedical Research Centre, and by the TBI-REPORTER Project, which is supported by a multi-funder consortium consisting of: UK Research and Innovation, National Institute for Health and Care Research; UK Department of Health and Social Care; UK Ministry of Defense, and Alzheimer's Research UK. He has no direct conflicts of interest with the submitted work but reports the following relationships outside the current work: consultancy and/or research grant support from NeuroTrauma Sciences, Lantmannen AB, GlaxoSmithKline Ltd, Integra Neurosciences, PressuraNeuro Ltd.

N.D.S. has received research operating funds from multiple granting agencies (Canada Foundation for Innovation, Canadian Institutes of Health Research, Mitacs, Ontario Brain Institute, US Department of Defense, WorkSafeBC, VGH + UBC Hospital Foundation) for research related to TBI diagnosis, prognosis, and treatment. He has received speaker fees for providing continuing medical education

on these topics. He serves as chair of the American Congress of Rehabilitation Medicine's Brain Injury Special Interest Group Task Force on Mild TBI (unpaid). He has served as an expert panel member for the Living Concussion Guidelines and as an external reviewer for other clinical practice guidelines on concussion/TBI (unpaid). He has provided expert testimony and medical-legal consulting in the past 5 years (<10% of total income).

A.R.F. reports research grant funding from US National Institutes of Health Neurological Disorders and Stroke (NINDS): R01NS122888, UH3NS106899, U24NS122732; the US Department of Veterans Affairs (VA): I01RX002245, I01RX002787, I01BX005871, I50BX005878; The Wings for Life Foundation; Craig H. Neilsen Foundation. He serves on the Data Safety Monitoring Board of Spine-X Inc.

T.J.B. has no funding disclosures or conflicts of interest to declare.

S.B. was supported by a Gates Cambridge Scholarship and is currently supported by a Paul & Daisy Soros Fellowship for New Americans; he has no conflicts of interest to disclose.

D.L.B. has no conflicts of interest to disclose but reports the following relationships outside of the current work: research currently funded by the US Department of Defense. Previous research funded also by NIH, DARPA, National Football League, Cure Alzheimer's Fund, Health South, Thrasher Foundation, BrightFocus, F-Prime & Burroughs Wellcome. Consulting: Advise Connect Inspire LLC, Algernon Pharmaceuticals, Avid Radiopharmaceuticals (Eli Lilly), Cirrito Holdings LLC, Escalent, Health Advances, Intellectual Ventures, iPerian, Kaigene, Kypha, Luna Innovations, Missouri State Public Defenders Office, Pfizer, Sage Therapeutics, Signum Nutralogix, St Louis Public Defenders Office, Stemedica, QualWorld. Equity: Inner Cosmos LLC. Royalties: Sales of Concussion Care Manual (Oxford University Press). Honoraria: Mary Ann Liebert, Inc. Publisher of *Journal of Neurotrauma* for services as Editor-in-Chief. Disclaimer statement: The opinions and assertions expressed herein are those of D.L.B. and do not necessarily reflect the official policy or position of the Uniformed Services University or the Department of Defense.

S.A.C. has no funding or conflicts of interest to declare.

A.E. has no funding to report and has direct conflicts of interest with the submitted work but reports the following relationships outside the current work: Consultancy to Lantmannen AB.

A.F. has no funding or conflicts of interest to declare.

G.G. has no funding to report or conflicts of interest to declare.

C.C.G. reports funding support by research grants from the following sources: NIH NINDS (R01 NS110757 2019-2024); NINDS (U54 NS121688 2021-2026); U.S.

Department of Defense CDMRP (TP210602 2022-2026); UCLA Brain Injury Research Center, UCLA Steve Tisch BrainSPORT program, Easton Clinic for Brain Health, UCLA CTSI NIH NCATS (UL1TR001881). He has no direct conflicts of interest with the submitted work but reports the following relationships outside the current work: Clinical Consultant (provide clinical care to patients): NBA, NFL-Neurological Care Program, NHL/NHLPA, Los Angeles Lakers, Los Angeles Chargers; Advisory Board (Non-compensated): Concussion in Sport Group, Major League Soccer, National Basketball Association, U.S. Soccer Federation; Stock Shareholder: Highmark Interactive stock options (2018).

F.L. is supported by the TBI-REPORTER multifunder grant. F.L. has no direct conflicts of interest with the submitted work but reports the following relationships outside the current work. Funding from the 2023 National Institute of Health and Care Excellence as Topic Adviser for the 2023 Head Injury (Assessment and Early Management) Guideline update (NG232). Funding from the National Institute of Health Research Health Technology Assessment Programme (two grants: Spinal Injury Study and Conservative Management of Traumatic Pneumothorax in the ED). Funding from National Health Service Trusts as Research Director for the Trauma Audit and Research Network.

R.M. reports research support from the Department of Defense, the National Institute of Child Health and Human Development, Abbott Laboratories, and the National Football League. She has no direct conflicts of interest with the submitted work, but reports the following relationships outside the current work: research funding from Abbott Laboratories.

A.M. is supported by the University of British Columbia (UBC) Institute of Mental Health (IMH) Marshall Fellows Program. She has no direct conflicts of interest with the submitted work.

K.E.M. is an employee of the Department of Defense, Army Medical Research and Development Command's Combat Casualty Care Research Program. His participation was supported by the performance of his duties in support of the Traumatic Brain Injury portfolio. He has no direct conflicts of interest with the submitted work. The views presented are those of the author and do not necessarily represent the views of DoD or its components.

C.S.R. was supported by research grants from the National Institutes of Health and the Department of Defense. She has no direct conflicts of interest with the submitted work.

A.T.E. has no direct funding conflicts of interest with the submitted work.

S.T. is partially supported through Biomedical Advanced Research and Development Authority of the U.S. Department of Health and Human Services (BARDA) and

U.S. Army Medical Research Acquisition Activity. She has no direct conflicts of interest with the submitted work.

J.K.Y. is supported by the Neurosurgery Research and Education Foundation Research Fellowship Grant (#A139203, disbursed to the institution [University of California, San Francisco]). He has no direct conflicts of interest with the submitted work.

Supplementary Material

Supplementary Data
Supplementary Figure S1
Supplementary Figure S2
Supplementary Table S1

References

1. Manley GT, Dams-O'Connor K, Alosco ML, et al. A New Framework for the Characterisation of Traumatic Brain Injury: Recommendations from the NINDS TBI Classification and Nomenclature Initiative. *Lancet Neurol* 2024;24(6):512–523.
2. MacDonald CL, Yuh EL, Vande Vyere T, et al. Neuroimaging Characterization of Traumatic Brain Injury: Recommendations from the 2024 NINDS TBI Classification and Nomenclature Initiative Imaging Working Group. *J Neurotrauma* 2025;42(13–14):1056–1064; doi: 10.1089/neu.2025.0079
3. Bazarian JJ, Zetterberg H, Buki A, et al. Blood-based biomarkers for improved characterization of TBI Recommendations from the 2024 NINDS TBI Classification and Nomenclature Initiative Blood-based Biomarkers Working Group. *J Neurotrauma* 2025;42(13–14):1065–1085; doi: 10.1089/neu.2024.0581
4. Nelson LD, Wilson L, Albrecht JS, et al. Toward More Holistic Early Traumatic Brain Injury Evaluation and Care: Recommendations from the NINDS TBI Classification and Nomenclature Initiative. *J Neurotrauma* 2025;42(13–14):1023–1037; doi: 10.1089/neu.2024.0569
5. Bragge P, McNett MM, Bayley M, et al. Starting with the end in mind—Recommendations to optimize implementation of a novel TBI classification from the 2024 NINDS TBI Classification and Nomenclature Workshop's Knowledge to Practice (K2P) Working Group. *J Neurotrauma* 2025;42(13–14):1096–1108; doi: 10.1089/neu.2024.0576
6. Corrigan JD, Alosco ML, van der Naalt J, et al. Retrospective Identification and characterization of traumatic brain injury – recommendations from the 2024 NINDS tbi classification and nomenclature initiative retrospective classification working group. *J Neurotrauma* 2025; 42(13–14):1086–1095; doi: 10.1089/neu.2024.0590
7. Teasdale G, Maas A, Lecky F, et al. The Glasgow Coma Scale at 40 years: Standing the test of time. *Lancet Neurol* 2014;13(8):844–854; doi: 10.1016/S1474-4422(14)70120-6
8. Matis G, Birbilis T. The glasgow Coma Scale—a brief review. Past, present, future. *Acta Neurol Belg* 2008;108(3):75–89.
9. Aguilar-Fuentes V, Orozco-Pa P, Jiménez-Ruiz A. The glasgow coma scale: 50-year anniversary. *Neurol Sci* 2024;45(6):2899–2901; doi: 10.1007/s10072-024-07432-9
10. Rimel RW, Jane JA, Edlich RF. An injury severity scale for comprehensive management of central nervous system trauma. *J Am Coll Emerg Physicians* 1979;8(2):64–67; doi: 10.1016/S0361-1124(79)80039-8
11. Rimel RW, Giordani B, Barth JT, et al. Disability caused by minor head injury. *Neurosurgery* 1981;9(3):221–228.
12. Rimel RW, Giordani B, Barth JT, et al. Moderate head injury: Completing the clinical spectrum of brain trauma. *Neurosurgery* 1982;11(3): 344–351; doi: 10.1227/00006123-198209000-00002
13. Holm L, David Cassidy J, Carroll L, et al.; Neurotrauma Task Force on Mild Traumatic Brain Injury of the WHO Collaborating Centre. Summary of the WHO collaborating centre for neurotrauma task force on mild traumatic brain injury. *J Rehabil Med* 2005;37(3):137–141; doi: 10.1080/16501970510027321
14. Menon DK, Schwab K, Wright DW, et al.; Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health. Position statement: Definition of traumatic brain injury. *Arch Phys Med Rehabil* 2010;91(11):1637–1640; doi: 10.1016/j.apmr.2010.05.017

15. Silverberg ND, Iverson GL, Cogan A, et al.; ACRM Mild TBI Diagnostic Criteria Expert Consensus Group. The American Congress of Rehabilitation Medicine diagnostic criteria for mild traumatic brain injury. *Arch Phys Med Rehabil* 2023;104(8):1343–1355; doi: 10.1016/j.apmr.2023.03.036
16. Giza CC, Hovda DA. The new neurometabolic cascade of concussion. *Neurosurgery* 2014;75(Suppl 4)(0 4):S24–S33; doi: 10.1227/NEU.0000000000000505
17. Wilde EA, McCauley SR, Barnes A, et al. Serial measurement of memory and diffusion tensor imaging changes within the first week following uncomplicated mild traumatic brain injury. *Brain Imaging Behav* 2012; 6(2):319–328; doi: 10.1007/s11682-012-9174-3
18. Lancaster MA, Olson DV, McCreary MA, et al. Acute white matter changes following sport-related concussion: A serial diffusion tensor and diffusion kurtosis tensor imaging study. *Hum Brain Mapp* 2016;37(11): 3821–3834; doi: 10.1002/hbm.23278
19. Lindsey HM, Hodges CB, Greer KM, et al. Diffusion-weighted imaging in mild traumatic brain injury: A systematic review of the literature. *Neuropsychol Rev* 2023;33(1):42–121; doi: 10.1007/s11065-021-09485-5
20. Tenovu O, Diaz-Arrastia R, Goldstein LE, et al. Assessing the severity of traumatic brain injury—time for a change? *J Clin Med* 2021;10(1): 148; doi: 10.3390/jcm10010148
21. Bodien YG, Barra A, Temkin NR, et al.; TRACK-TBI Investigators. Diagnosing level of consciousness: The limits of the Glasgow Coma Scale total score. *J Neurotrauma* 2021;38(23):3295–3305; doi: 10.1089/neu.2021.0199
22. Borgialli DA, Mahajan P, Hoyle JD, et al.; Pediatric Emergency Care Applied Research Network (PECARN). Performance of the pediatric Glasgow Coma Scale score in the evaluation of children with blunt head trauma. *Acad Emerg Med* 2016;23(8):878–884; doi: 10.1111/acem.13014
23. Gardner RC, Dams-O'Connor K, Morrissey MR, et al. Geriatric traumatic brain injury: Epidemiology, outcomes, knowledge gaps, and future directions. *J Neurotrauma* 2018;35(7):889–906; doi: 10.1089/neu.2017.5371
24. Anonymous. Overview | Head Injury: Assessment and Early Management | Guidance | NICE. 2023. Available from: <https://www.nice.org.uk/guidance/ng232> [Last accessed June 3, 2024].
25. Steyerberg EW, Wieggers E, Sewalt C, et al.; CENTER-TBI Participants and Investigators. Case-mix, care pathways, and outcomes in patients with traumatic brain injury in CENTER-TBI: A European prospective, multi-centre, longitudinal, cohort study. *Lancet Neurol* 2019;18(10):923–934; doi: 10.1016/S1474-4422(19)30232-7
26. Van Veen E, Van Der Jagt M, Citerio G, et al.; CENTER-TBI investigators and participants. Occurrence and timing of withdrawal of life-sustaining measures in traumatic brain injury patients: A CENTER-TBI study. *Intensive Care Med* 2021;47(10):1115–1129; doi: 10.1007/s00134-021-06484-1
27. Malhotra AK, Shakil H, Smith CW, et al. Withdrawal of life-sustaining treatment for pediatric patients with severe traumatic brain injury. *JAMA Surg* 2024;159(3):287–296; doi: 10.1001/jamasurg.2023.6531
28. Sanders WR, Barber JK, Temkin NR, et al. Recovery potential in patients who died after withdrawal of life-sustaining treatment: A TRACK-TBI propensity score analysis. *J Neurotrauma* 2024;41(19–20):2336–2348; doi: 10.1089/neu.2024.0014
29. Marmarou A, Lu J, Butcher I, et al. Prognostic value of the Glasgow Coma Scale and pupil reactivity in traumatic brain injury assessed pre-hospital and on enrollment: An IMPACT Analysis. *J Neurotrauma* 2007; 24(2):270–280; doi: 10.1089/neu.2006.0029
30. Phillips SS, Mueller CM, Nogueira RG, et al. A systematic review assessing the current state of automated pupillometry in the NeuroICU. *Neurocrit Care* 2019;31(1):142–161; doi: 10.1007/s12028-018-0645-2
31. Brennan PM, Murray GD, Teasdale GM. Simplifying the use of prognostic information in traumatic brain injury. Part 1: The GCS-Pupils score: An extended index of clinical severity. *J Neurosurg* 2018;128(6): 1612–1620; doi: 10.3171/2017.12.JNS172780
32. Vreeburg RJG, Leeuwen FD, van Manley GT, et al. Validation of the GCS-Pupil scale in traumatic brain injury incremental prognostic performance of pupillary reactivity with GCS in the prospective observational cohorts CENTER-TBI and TRACK-TBI. 2024;2024(06.05.24308424); doi: 10.1101/2024.06.05.24308424
33. Ercole A, Dixit A, Nelson DW, et al.; CENTER-TBI Investigators and Participants. Imputation strategies for missing baseline neurological assessment covariates after traumatic brain injury: A CENTER-TBI study. *PLoS One* 2021;16(8):e0253425; doi: 10.1371/journal.pone.0253425
34. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain injury: Development and international validation of prognostic scores based on admission characteristics. *PLoS Med* 2008; 5(8):e165; doi: 10.1371/journal.pmed.0050165
35. Perel P, Arango M, Clayton T, et al.; MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: Practical prognostic models based on large cohort of international patients. *Bmj* 2008; 336(7641):425–429; doi: 10.1136/bmj.39461.643438.25
36. Ahmadi S, Sarveazad A, Babahajian A, et al. Comparison of Glasgow Coma Scale and full outline of UnResponsiveness score for prediction of in-hospital mortality in traumatic brain injury patients: A systematic review and meta-analysis. *Eur J Trauma Emerg Surg* 2023;49(4): 1693–1706; doi: 10.1007/s00068-022-02111-w
37. Mikolić A, Steyerberg EW, Polinder S, et al. Prognostic models for global functional outcome and post-concussion symptoms following mild traumatic brain injury: A collaborative European neurotrauma effectiveness research in traumatic brain injury (CENTER-TBI) study. *J Neurotrauma* 2023;40(15–16):1651–1670; doi: 10.1089/neu.2022.0320
38. Silverberg ND, Gardner AJ, Brubacher JR, et al. Systematic review of multivariable prognostic models for mild traumatic brain injury. *J Neurotrauma* 2015;32(8):517–526; doi: 10.1089/neu.2014.3600
39. Yang Y-C, Lin P-C, Liu C-Y, et al. Prehospital shock index multiplied by avpu scale as a predictor of clinical outcomes in traumatic injury. *Shock* 2022;58(6):524–533; doi: 10.1097/SHK.0000000000002018
40. Clark A, Das JM, Mesfin FB. Trauma Neurological Exam. In: StatPearls Publishing: Treasure Island (FL); 2024.
41. Ponsford J, Janzen S, McIntyre A, et al.; INCOG Expert Panel. INCOG recommendations for management of cognition following traumatic brain injury, Part I: Posttraumatic amnesia/delirium. *J Head Trauma Rehabil* 2014;29(4):307–320; doi: 10.1097/HTR.0000000000000074
42. Spiteri C, Ponsford J, Jones H, et al. Comparing the westmead posttraumatic amnesia scale, galveston orientation and amnesia test, and confusion assessment protocol as measures of acute recovery following traumatic brain injury. *J Head Trauma Rehabil* 2021;36(3):156–163; doi: 10.1097/HTR.0000000000000607
43. Friedland D, Swash M. Post-traumatic amnesia and confusional state: Hazards of retrospective assessment. *J Neurol Neurosurg Psychiatry* 2016;87(10):1068–1074; doi: 10.1136/jnnp-2015-312193
44. McCarter RJ, Walton NH, Moore C, et al. PTA testing, the westmead post traumatic amnesia scale and opiate analgesia: A cautionary note. *Brain Inj* 2007;21(13–14):1393–1397; doi: 10.1080/02699050701793793
45. Haydel MJ, Preston CA, Mills TJ, et al. Indications for computed tomography in patients with minor head injury. *N Engl J Med* 2000;343(2): 100–105; doi: 10.1056/NEJM200007133430204
46. Roberts CM, Spitz G, Ponsford JL. Comparing prospectively recorded posttraumatic amnesia duration with retrospective accounts. *J Head Trauma Rehabil* 2016;31(2):E71–E77; doi: 10.1097/HTR.0000000000000154
47. Lecky FE, Otesile O, Marincowitz C, et al.; CENTER-TBI Participants and Investigators. The burden of traumatic brain injury from low-energy falls among patients from 18 countries in the CENTER-TBI Registry: A comparative cohort study. *PLoS Med* 2021;18(9):e1003761; doi: 10.1371/journal.pmed.1003761
48. Maas AIR, Menon DK, Adelson PD, et al.; INtBIR Participants and Investigators. Traumatic brain injury: Integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol* 2017;16(12): 987–1048; doi: 10.1016/S1474-4422(17)30371-X
49. Lingsma HF, Yue JK, Maas AIR, et al.; TRACK-TBI Investigators. Outcome prediction after mild and complicated mild traumatic brain injury: External validation of existing models and identification of new predictors using the TRACK-TBI pilot study. *J Neurotrauma* 2015;32(2):83–94; doi: 10.1089/neu.2014.3384
50. Mikolić A, Polinder S, Steyerberg EW, et al.; Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) Study Participants and Investigators. Prediction of global functional outcome and post-concussive symptoms after mild traumatic brain injury: External validation of prognostic models in the collaborative European neurotrauma effectiveness research in traumatic brain injury (CENTER-TBI) study. *J Neurotrauma* 2021;38(2):196–209; doi: 10.1089/neu.2020.7074
51. Le Sage N, Chauny J-M, Berthelot S, et al. Post-Concussion symptoms rule: Derivation and validation of a clinical decision rule for early prediction of persistent symptoms after a mild traumatic brain injury. *J Neurotrauma* 2022;39(19–20):1349–1362; doi: 10.1089/neu.2022.0026
52. Zemek R, Barrowman N, Freedman SB, et al.; Pediatric Emergency Research Canada (PERC) Concussion Team. Clinical risk score for persistent postconcussion symptoms among children with acute concussion in the ED. *JAMA* 2016;315(10):1014–1025; doi: 10.1001/jama.2016.1203

53. Miller SM, Valovich McLeod TC, Zaslow TL, et al. Utility of a clinical prediction tool for persisting postconcussive symptoms in a multicenter sample of youth athletes with concussion: The sport concussion outcomes in pediatrics (SCOPE) study. *Am J Sports Med* 2023;51(13): 3546–3553; doi: 10.1177/03635465231201610
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. *Lancet Neurol* 2017;16(7):532–540; doi: 10.1016/S1474-4422(17)30117-5
55. Stulemeijer M, Van Der Werf S, Borm GF, et al. Early prediction of favourable recovery 6 months after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2008;79(8):936–942; doi: 10.1136/jnnp.2007.131250
56. Iverson GL, Gardner AJ, Terry DP, et al. Predictors of clinical recovery from concussion: A systematic review. *Br J Sports Med* 2017;51(12): 941–948; doi: 10.1136/bjsports-2017-097729
57. Cnossen MC, Van Der Naalt J, Spikman JM, et al. Prediction of persistent post-concussion symptoms after mild traumatic brain injury. *J Neurotrauma* 2018;35(22):2691–2698; doi: 10.1089/neu.2017.5486
58. Mikolić A, Brasher PMA, Brubacher JR, et al. External validation of the post-concussion symptoms rule for predicting mild traumatic brain injury outcome. *J Neurotrauma* 2024;41(15–16):1929–1936; doi: 10.1089/neu.2023.0484
59. Mac Donald CL, Adam OR, Johnson AM, et al. Acute post-traumatic stress symptoms and age predict outcome in military blast concussion. *Brain* 2015;138(Pt 5):1314–1326; doi: 10.1093/brain/awv038
60. Brooks BL, Daya H, Khan S, et al. Cognition in the emergency department as a predictor of recovery after pediatric mild traumatic brain injury. *J Int Neuropsychol Soc* 2016;22(4):379–387; doi: 10.1017/S1355617715001368
61. Ponsford J, Cameron P, Fitzgerald M, et al. Predictors of postconcussive symptoms 3 months after mild traumatic brain injury. *Neuropsychology* 2012;26(3):304–313; doi: 10.1037/a0027888
62. Luoto TM, Silverberg ND, Kataja A, et al. Sport concussion assessment tool 2 in a civilian trauma sample with mild traumatic brain injury. *J Neurotrauma* 2014;31(8):728–738; doi: 10.1089/neu.2013.3174
63. Bazarian JJ, Wong T, Harris M, et al. Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. *Brain Inj* 1999;13(3):173–189; doi: 10.1080/026990599121692
64. Sheedy J, Harvey E, Faux S, et al. Emergency department assessment of mild traumatic brain injury and the prediction of postconcussive symptoms: A 3-Month prospective study. *J Head Trauma Rehabil* 2009; 24(5):333–343; doi: 10.1097/HTR.0b013e3181aea51f
65. Norris JN, Carr W, Herzig T, et al. ANAM4 TBI Reaction Time-Based tests have prognostic utility for acute concussion. *Mil Med* 2013;178(7): 767–774; doi: 10.7205/MILMED-D-12-00493
66. Hannah T, Dreher N, Li AY, et al. Assessing the predictive value of primary evaluation with the Immediate Post-Concussion Assessment and Cognitive Test following head injury. *J Neurosurg Pediatr* 2020;26(2): 171–178; doi: 10.3171/2020.2.PEDS19709
67. Lau BC, Collins MW, Lovell MR. Sensitivity and specificity of subacute computerized neurocognitive testing and symptom evaluation in predicting outcomes after sports-related concussion. *Am J Sports Med* 2011;39(6):1209–1216; doi: 10.1177/0363546510392016
68. Hanks RA, Millis SR, Ricker JH, et al. The predictive validity of a brief inpatient neuropsychologic battery for persons with traumatic brain injury. *Arch Phys Med Rehabil* 2008;89(5):950–957; doi: 10.1016/j.apmr.2008.01.011
69. Williams MW, Rapport LJ, Hanks RA, et al. Incremental validity of neuropsychological evaluations to computed tomography in predicting long-term outcomes after traumatic brain injury. *Clin Neuropsychol* 2013;27(3):356–375; doi: 10.1080/13854046.2013.765507
70. Sherer M, Novack TA, Sander AM, et al. Neuropsychological assessment and employment outcome after traumatic brain injury: A review. *Clin Neuropsychol* 2002;16(2):157–178; doi: 10.1076/clin.16.2.157.13238
71. Whelan BM, Gause EL, Ortega JD, et al. King-Devick testing and concussion recovery time in collegiate athletes. *J Sci Med Sport* 2022; 25(11):930–934; doi: 10.1016/j.jsams.2022.08.012
72. Vanderhorst M, Rawlings A, Germansky M, et al. Prognostic utility of oculomotor assessments in determining return-to-learn time in acutely concussed college student-athletes: A pilot study. *Neurotrauma Rep* 2023;4(1):515–521; doi: 10.1089/neur.2023.0027
73. Price AM, Knell G, Caze TJ, et al. Exploring vestibular/ocular and cognitive dysfunction as prognostic factors for protracted recovery in sports-related concussion patients aged 8 to 12 Years. *Clin J Sport Med* 2022;32(4):408–414; doi: 10.1097/JSM.0000000000000975
74. Anzalone AJ, Blueitt D, Case T, et al. A positive vestibular/ocular motor screening (VOMS) is associated with increased recovery time after sports-related concussion in youth and adolescent athletes. *Am J Sports Med* 2017;45(2):474–479; doi: 10.1177/0363546516668624
75. Wang EX, Hwang CE, Nguyen JN, et al. Factors associated with a prolonged time to return to play after a concussion. *Am J Sports Med* 2022;50(6):1695–1701; doi: 10.1177/03635465221083646
76. Knell G, Caze T, Burkhart SO. Evaluation of the vestibular and ocular motor screening (VOMS) as a prognostic tool for protracted recovery following paediatric sports-related concussion. *BMJ Open Sport Exerc Med* 2021;7(1):e000970; doi: 10.1136/bmjsem-2020-000970
77. Whitney SL, Eagle SR, Marchetti G, et al.; CARE Consortium Investigators. Association of acute vestibular/ocular motor screening scores to prolonged recovery in collegiate athletes following sport-related concussion. *Brain Inj* 2020;34(6):840–845; doi: 10.1080/02699052.2020.1755055
78. Leddy JJ, Hinds AL, Miecznikowski J, et al. Safety and prognostic utility of provocative exercise testing in acutely concussed adolescents: A randomized trial. *Clin J Sport Med* 2018;28(1):13–20; doi: 10.1097/JSM.0000000000000431
79. Haider MN, Leddy JJ, Wilber CG, et al. The predictive capacity of the buffalo concussion treadmill test after sport-related concussion in adolescents. *Front Neurol* 2019;10:395; doi: 10.3389/fneur.2019.00395
80. Jain D, Arbogast KB, McDonald CC, et al. Eye tracking metrics differences among uninjured adolescents and those with acute or persistent post-concussion symptoms. *Optom Vis Sci* 2022;99(8):616–625; doi: 10.1097/OPX.0000000000001921
81. Howell DR, Mayer AR, Master CL, et al. Prognosis for persistent post concussion symptoms using a multifaceted objective gait and balance assessment approach. *Gait Posture* 2020;79:53–59; doi: 10.1016/j.gaitpost.2020.04.013
82. Howell DR, Brilliant A, Berkstresser B, et al. The association between dual-task gait after concussion and prolonged symptom duration. *J Neurotrauma* 2017;34(23):3288–3294; doi: 10.1089/neu.2017.5191
83. Sufrinko A, McAllister-Deitrick J, Womble M, et al. Do sideline concussion assessments predict subsequent neurocognitive impairment after sport-related concussion? *J Athl Train* 2017;52(7):676–681; doi: 10.4085/1062-6050-52.4.01
84. Kontos AP, Monti K, Eagle SR, et al. Test-retest reliability of the Vestibular Ocular Motor Screening (VOMS) tool and modified Balance Error Scoring System (mBESS) in US military personnel. *J Sci Med Sport* 2021;24(3):264–268; doi: 10.1016/j.jsams.2020.08.012
85. Mac Donald CL, Johnson AM, Wierzechowski L, et al. Outcome trends after US military concussive traumatic brain injury. *J Neurotrauma* 2017;34(14):2206–2219; doi: 10.1089/neu.2016.4434
86. Van Leeuwen N, Lingsma HF, Perel P, et al.; Trauma Audit and Research Network. prognostic value of major extracranial injury in traumatic brain injury: An individual patient data meta-analysis in 39 274 Patients. *Neurosurgery* 2012;70(4):811–818; discussion 818; doi: 10.1227/NEU.0b013e318235d640
87. 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. *Neurotrauma Rep* 2020;1(1):32–41; doi: 10.1089/neur.2020.0004
88. Gravestijn BY, Sewalt CA, Stocchetti N, et al.; CENTER-TBI collaborators. Prehospital management of traumatic brain injury across europe: A CENTER-TBI Study. *Prehosp Emerg Care* 2021;25(5):629–643; doi: 10.1080/10903127.2020.1817210
89. McDonald SJ, Sun M, Agoston DV, et al. The effect of concomitant peripheral injury on traumatic brain injury pathobiology and outcome. *J Neuroinflammation* 2016;13(1):90; doi: 10.1186/s12974-016-0555-1
90. Roberts CJ, Barber J, Temkin NR, et al.; Transforming Clinical Research and Knowledge in TBI (TRACK-TBI) Investigators. Clinical outcomes after traumatic brain injury and exposure to extracranial surgery: A TRACK-TBI Study. *JAMA Surg* 2024;159(3):248–259; doi: 10.1001/jamasurg.2023.6374
91. Anonymous. Abbreviated Injury Scale (AIS). n.d. Available from: <https://www.aaam.org/abbreviated-injury-scale-ais/> [Last accessed Last, accessed].
92. Foreman BP, Caesar RR, Parks J, et al. Usefulness of the abbreviated injury score and the injury severity score in comparison to the Glasgow Coma Scale in predicting outcome after traumatic brain injury. *J Trauma* 2007;62(4):946–950; doi: 10.1097/01.ta.0000229796.14717.3a
93. Chesnut RM, Marshall LF, Klauber MR, et al. The role of secondary brain injury in determining outcome from severe head injury. *J Trauma* 1993;34(2):216–222; doi: 10.1097/00005373-199302000-00006

94. Shibahashi K, Sugiyama K, Okura Y, et al. Defining hypotension in patients with severe traumatic brain injury. *World Neurosurg* 2018;120:e667–e674; doi: 10.1016/j.wneu.2018.08.142
95. Huang H-K, Liu C-Y, Tzeng I-S, et al. The association between blood pressure and in-hospital mortality in traumatic brain injury: Evidence from a 10-year analysis in a single-center. *Am J Emerg Med* 2022;58:265–274; doi: 10.1016/j.ajem.2022.05.047
96. Rezoagli E, Petrosino M, Rebora P, et al.; CENTER-TBI, OzENTER-TBI Participants and Investigators. High arterial oxygen levels and supplemental oxygen administration in traumatic brain injury: Insights from CENTER-TBI and OzENTER-TBI. *Intensive Care Med* 2022;48(12):1709–1725; doi: 10.1007/s00134-022-06884-x
97. Saxena M, Young P, Pilcher D, et al. Early temperature and mortality in critically ill patients with acute neurological diseases: Trauma and stroke differ from infection. *Intensive Care Med* 2015;41(5):823–832; doi: 10.1007/s00134-015-3676-6
98. American College of Surgeons Trauma Programs 2024. Best Practice Guidelines. The Management of Traumatic Brain Injury. Available from: <https://www.facs.org/media/vgfgjpfk/best-practices-guidelines-traumatic-brain-injury.pdf> [Last accessed: January 16, 2025].
99. Flynn JT, Kaelber DC, Baker-Smith CM, et al.; SUBCOMMITTEE ON SCREENING AND MANAGEMENT OF HIGH BLOOD PRESSURE IN CHILDREN. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics* 2017;140(3):e20171904; doi: 10.1542/peds.2017-1904
100. Shypailo R. Age-Based Pediatric Blood Pressure Reference Charts. 2018. Available from: <https://www.bcm.edu/bodycomplab/BPappZjs/BPvAgeAPPz.html> [Last accessed: October 10, 2024].
101. Svedung Wettervik T, Velle F, Hånell A, et al. ICP, PRx, CPP, and ΔCPPopt in pediatric traumatic brain injury: The combined effect of insult intensity and duration on outcome. *Childs Nerv Syst* 2023;39(9):2459–2466; doi: 10.1007/s00381-023-05982-5
102. Bb A, Yi C, Lm G, et al. Age-specific cerebral perfusion pressure thresholds and survival in children and adolescents with severe traumatic brain injury*. *Pediatr Crit Care Med J Soc Crit Care Med World Fed Pediatr Intensive Crit Care Soc* 2014;15(1); doi: 10.1097/PCC.0b013e3182a556ea
103. Laing J, Gabbe B, Chen Z, et al. Risk factors and prognosis of early post-traumatic seizures in moderate to severe traumatic brain injury. *JAMA Neurol* 2022;79(4):334–341; doi: 10.1001/jamaneurol.2021.5420
104. Hukkelhoven CWM, Steyerberg EW, Rampen AJ, et al. Patient age and outcome following severe traumatic brain injury: An analysis of 5600 patients. *J Neurosurg* 2003;99(4):666–673; doi: 10.3171/jns.2003.99.4.0666
105. Mushkudiani NA, Engel DC, Steyerberg EW, et al. Prognostic Value of Demographic Characteristics in Traumatic Brain Injury: Results from The IMPACT Study. *J Neurotrauma* 2007;24(2):259–269; doi: 10.1089/neu.2006.0028
106. Centers for Disease Control and Prevention. (2018). Report to Congress: The Management of Traumatic Brain Injury in Children, National Center for Injury Prevention and Control; Division of Unintentional Injury Prevention. Atlanta, GA.
107. Crowe LM, Catroppa C, Babl FE, et al. Timing of traumatic brain injury in childhood and intellectual outcome. *J Pediatr Psychol* 2012;37(7):745–754; doi: 10.1093/jpepsy/js070
108. Kirkman MA, Jenks T, Bouamra O, et al. Increased mortality associated with cerebral contusions following trauma in the elderly: Bad patients or bad management? *J Neurotrauma* 2013;30(16):1385–1390; doi: 10.1089/neu.2013.2881
109. Stocchetti N, Paternò R, Citerio G, et al. Traumatic brain injury in an aging population. *J Neurotrauma* 2012;29(6):1119–1125; doi: 10.1089/neu.2011.1995
110. Swart KM, Van Der Heijden AA, Blom MT, et al. Identification of frailty in primary care: Accuracy of electronically derived measures. *Br J Gen Pract* 2023;73(735):e752–e759; doi: 10.3399/BJGP.2022.0574
111. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173(5):489–495; doi: 10.1503/cmaj.050051
112. Subramaniam S, Aalberg JJ, Soriano RP, et al. New 5-factor modified frailty index using American College of Surgeons NSQIP Data. *J Am Coll Surg* 2018;226(2):173–181.e8; doi: 10.1016/j.jamcollsurg.2017.11.005
113. Panchangam C, White DA, Goudar S, et al. Translation of the frailty paradigm from older adults to children with cardiac disease. *Pediatr Cardiol* 2020;41(5):1031–1041; doi: 10.1007/s00246-020-02354-7
114. Maragkos GA, Matsoukas S, Cho LD, et al. Comparison of frailty indices and the Charlson Comorbidity Index in traumatic brain injury. *J Head Trauma Rehabil* 2023;38(3):E177–E185; doi: 10.1097/HTR.0000000000000832
115. Tang OY, Shao B, Kimata AR, et al. The impact of frailty on traumatic brain injury outcomes: An analysis of 691 821 nationwide cases. *Neurosurgery* 2022;91(5):808–820; doi: 10.1227/neu.0000000000002116
116. Galimberti S, Graziano F, Maas AIR, et al.; CENTER-TBI and TRACK-TBI participants and investigators. Effect of frailty on 6-month outcome after traumatic brain injury: A multicentre cohort study with external validation. *Lancet Neurol* 2022;21(2):153–162; doi: 10.1016/S1474-4422(21)00374-4
117. Zacchetti L, Longhi L, Zangari R, et al. Clinical frailty scale as a predictor of outcome in elderly patients affected by moderate or severe traumatic brain injury. *Front Neurol* 2023;14:1021020; doi: 10.3389/fneur.2023.1021020
118. Herklots MW, Kroon M, Roks G, et al. Poor outcome in frail elderly patient after severe TBI. *Brain Inj* 2022;36(9):1118–1122; doi: 10.1080/02699052.2022.2109731
119. Mollaveya T, Hurst M, Chan V, et al. Pre-injury health status and excess mortality in persons with traumatic brain injury: A decade-long historical cohort study. *Prev Med* 2020;139:106213; doi: 10.1016/j.ypmed.2020.106213
120. Max JE, Friedman K, Wilde EA, et al. Psychiatric disorders in children and adolescents 24 months after mild traumatic brain injury. *J Neuropsychiatry Clin Neurosci* 2015;27(2):112–120; doi: 10.1176/appi.neuropsych.13080190
121. Maegele M. Coagulopathy and progression of intracranial hemorrhage in traumatic brain injury: Mechanisms, impact, and therapeutic considerations. *Neurosurgery* 2021;89(6):954–966; doi: 10.1093/neuros/nyab358
122. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD The PHQ primary care study. *JAMA* 1999;282(18):1737–1744; doi: 10.1001/jama.282.18.1737
123. Spitzer RL, Kroenke K, Williams JBW, et al. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Arch Intern Med* 2006;166(10):1092–1097; doi: 10.1001/archinte.166.10.1092
124. Hoge CW, Riviere LA, Wilk JE, et al. The prevalence of post-traumatic stress disorder (PTSD) in US combat soldiers: A head-to-head comparison of DSM-5 versus DSM-IV-TR symptom criteria with the PTSD checklist. *Lancet Psychiatry* 2014;1(4):269–277; doi: 10.1016/S2215-0366(14)70235-4
125. Temkin N, Machamer J, Dikmen S, et al.; TRACK-TBI Investigators. Risk factors for high symptom burden three months after traumatic brain injury and implications for clinical trial design: A transforming research and clinical knowledge in traumatic brain injury study. *J Neurotrauma* 2022;39(21–22):1524–1532; doi: 10.1089/neu.2022.0113
126. Yue J, Krishnan N, Kanter J, et al.; TRACK-TBI Investigators. Neuroimaging in the emergency department is a predictor of traumatic brain injury intervention and outcome: A TRACK-TBI pilot study. *J Clin Med* 2023;12(5):2024; doi: 10.3390/jcm12052024
127. Bhattacharyay S, Caruso PF, Åkerlund C, et al.; CENTER-TBI investigators and participants. Mining the contribution of intensive care clinical course to outcome after traumatic brain injury. *NPJ Digit Med* 2023;6(1):154; doi: 10.1038/s41746-023-00895-8
128. Bhattacharyay S, Beqiri E, Zuercher P, et al. Therapy intensity level scale for traumatic brain injury: Clinimetric assessment on neuro-monitored patients across 52 European intensive care units. *J Neurotrauma* 2024;41(7–8):887–909; doi: 10.1089/neu.2023.0377
129. Tritt A, Yue JK, Ferguson AR, et al.; TRACK-TBI Investigators. Data-driven distillation and precision prognosis in traumatic brain injury with interpretable machine learning. *Sci Rep* 2023;13(1):21200; doi: 10.1038/s41598-023-48054-z
130. Khalili H, Rismani M, Nematollahi MA, et al. Prognosis prediction in traumatic brain injury patients using machine learning algorithms. *Sci Rep* 2023;13(1):960; doi: 10.1038/s41598-023-28188-w
131. Kaplan AD, Cheng Q, Mohan KA, et al. Mixture model framework for traumatic brain injury prognosis using heterogeneous clinical and outcome data. *IEEE J Biomed Health Inform* 2022;26(3):1285–1296; doi: 10.1109/JBHI.2021.3099745
132. Galos P, Hult L, Zachariah D, et al. Machine learning based prediction of imminent ICP insults during neurocritical care of traumatic brain injury. *Neurocrit Care* 2024; doi: 10.1007/s12028-024-02119-7
133. Carra G, Güiza F, Piper I, et al.; CENTER-TBI High-Resolution ICU (HR ICU) Sub-Study Participants and Investigators. Development and external validation of a machine learning model for the early prediction of doses of harmful intracranial pressure in patients with severe traumatic brain injury. *J Neurotrauma* 2023;40(5–6):514–522; doi: 10.1089/neu.2022.0251

134. Gulamali F, Jayaraman P, Sawant AS, et al. Derivation, external and clinical validation of a deep learning approach for detecting intracranial hypertension. *NPJ Digit Med* 2024;7(1):233; doi: 10.1038/s41746-024-01227-0
135. Rohaut B, Calligaris C, Hermann B, et al. Multimodal assessment improves neuroprognosis performance in clinically unresponsive critical-care patients with brain injury. *Nat Med* 2024;30(8):2349–2355; doi: 10.1038/s41591-024-03019-1
136. Appiah Balaji NN, Beaulieu CL, Bogner J, et al. Traumatic brain injury rehabilitation outcome prediction using machine learning methods. *Arch Rehabil Res Clin Transl* 2023;5(4):100295; doi: 10.1016/j.arrct.2023.100295
137. Van Der Naalt J, Van Zomeren AH, Sluiter WJ, et al. One year outcome in mild to moderate head injury: The predictive value of acute injury characteristics related to complaints and return to work. *J Neurol Neurosurg Psychiatry* 1999;66(2):207–213; doi: 10.1136/jnnp.66.2.207
138. Ponsford JL, Spitz G, McKenzie D. Using Post-Traumatic amnesia to predict outcome after traumatic brain injury. *J Neurotrauma* 2016;33(11):997–1004; doi: 10.1089/neu.2015.4025
139. Vile AR, Jang K, Gourlay D, et al. Posttraumatic Amnesia: A systematic review and Meta-Analysis. Proposal for a new severity classification. *World Neurosurg* 2022;162:e369–e393; doi: 10.1016/j.wneu.2022.03.018