Supplemental Digital Content 5. Synthesis of results for secondary outcomes

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| **First author and year of publication of review** | **Studies (n)**  (RCT; prospective;  retrospective; other) | **Patients**  **(n)** | **AMSTAR-2** | **Measures of association on secondary outcomes (95% CI)** | | **Heterogeneity**  χ2, **Q or I2** | **Reported risk of bias in original studies** | | **Reported GRADE** |
| **Head CT in adults with acute mild TBI at low risk on a validated clinical decision rule** | | | | | | | | | |
| Neurosurgical intervention | | | | | | | | | |
| Pandor et al. 2011  *CCHR (high risk criteria)*  *CHIP*  *New Orleans Criteria*  *NEXUS-II* | 0; 3; 1; 0  0; 1; 0; 0  0; 3; 1; 0  0; 1; 0; 0 | 14,023  3,181  11,324  7,955 | Moderate | P\*: 0 to 0.03%  P\*: 0%  P\*: 0 to 0.04%  P\*: 0% | | NA |  | | NR |
| **Routine repeat head CT in absence of neurological deterioration in adults with acute mild complicated TBI** | | | | | | | | | |
| Change in management following repeat CT | | | | | | | | | |
| Almenawer et al. 2013 | NR | NR | Critically low | P: 0.6% (0.3-1.0%) | | I2=21.2% |  | | NR |
| Reljic et al. 2014  *Prospective*  *Retrospective* | 0; 5; 0; 0  0; 0; 9; 0 |  | Critically low | P: 2.3% (0.3-6.3%)  P: 3.9% (2.3-5.7%) | | I2=83.2%  I2=69.3% |  | | Low |
| Change in ICP monitoring | | | | | | | | | |
| Reljic et al. 2014 | 0; 0; 7; 0 | 1,369 | Critically low | P : 1.2% (0.4-2.4%) | | I2=60.7% |  | | Low |
| Neurosurgical intervention | | | | | | | | | |
| Stippler et al. 2012 | 0; 8; 7; 4 | 1,630 | Critically low | | P: 2.4% | NR | Low: 0/19 | NR | |
| Almenawer et al. 2013 | 0; 8; 4; 0 | 2,693 | Critically low | | P: 0.6% (0.3 to 0.10%) | NR | Moderate to high | NR | |
| Reljic et al. 2014  *Prospective*  *Retrospective* | 0; 1; 0; 0  0; 0; 9; 0 | 1,958 | Low | | P: 1.5% (0.2 to 5.5%)  P: 2.4% (1.4 to 3.5%) | NA  I2=50.4% | NR | Low | |
| **Routine repeat head CT in absence of neurological deterioration in adults with acute mild TBI on anticoagulant or antiplatelet therapy** | | | | | | | | | |
| Clinically relevant poor outcomes (neurosurgical intervention or death) | | | | | | | | | |
| Chauny et al. 2016 | 0; 3; 4; 0 | 1,594 | Critically low | | P: 0.13% (0.02-0.45) | NR | Low, moderate: 2/7 | NR | |
| **Plasma transfusion in adults with traumatic brain injury** | | | | | | | | | |
| Mortality | | | | | | | | | |
| Yang et al. 2012 | 1; 0; 0; 0 | 90 | Moderate | Mortality was significantly more common in the frozen plasma group | | NA | NR | | NR |
| **Antibiotic prophylaxis in adults with basal skull fractures without evidence of cerebrospinal fluid leakage** | | | | | | | | | |
| Mortality | | | | | | | | | |
| Ratilal et al. 2015  *All-cause*  *Meningitis-related* | 4; 0; 0; 0  4; 0; 0; 0 | 208  208 | Moderate | OR: 1.68 (0.41-6.95)  OR: 1.03 (0.14-7.40) | | I2=0%  I2=0% |  | | Moderate |
| **Therapeutic hypothermia in adults with acute traumatic brain injury** | | | | | | | | | |
| Mortality | | | | | | | | | |
| Henderson et al. 2003 | 8; 0; 0; 0 | 748 | Critically low | OR: 0.81 (0.59-1.13) | | P=0.19 |  | | NR |
| McIntyre et al. 2003 | 12; 0; 0; 0 | 1,069 | Low | RR: 0.81 (0.69-0.96) | | Q=8.12 |  | | NR |
| Bratton et al. 2007 | 6; 0; 0; 0 | 694 | Critically low | RR: 0.76 (0.55-1.05) | | I2=34% |  | | NR |
| Peterson et al. 2008 | 8; 0; 0; 0 | 781 | Low | RR: 0.80 (0.59-1.09) | | I2=27.8% |  | | NR |
| Sydenham et al. 2009  *All studies*  *High quality* | 20; 0; 0; 0  8; 0; 0; 0 | 1,382  686 | Low | OR: 0.76 (0.60-0.97)  OR: 0.96 (0.68-1.35) | | I2=0%  I2=0% |  | | NR |
| Fox et al. 2010 | 12; 0; 0; 0 | 1,327 | Moderate | RR: 0.73 (0.62-0.85) | | I2=0% |  | | NR |
| Georgiou et al. 2013  *All studies*  *High quality* | 18; 0; 0; 0  3; 0; 0; 0 | 1,827  690 | Low | RR: 0.84 (0.72-0.98)  RR: 1.28 (0.89-1.83) | | I2=26%  I2=9% |  | | Low |
| Crossley et al. 2014  *All studies*  *High quality* | 18; 0; 0; 0  14; 0; 0; 0 | 1,839  918 | High | RR: 1.31 (1.13-1.52)  RR: 1.62 (1.30-2.01) | | I2=24%  I2=0% |  | | NR |
| Li et al. 2014 | 12; 1; 0; 0 | 1,152 | Critically low | RR: 0.86 (0.73-1.01) | | I2=21% |  | | NR |
| Zhu et al. 2016  *All studies*  *High quality* | 10; 0; 0; 0  5; 0; 0; 0 | 1,621  781 | Moderate | RR: 0.96 (0.76-1.23)  RR: 1.22 (0.97-1.54) | | I2=48%  I2=0% |  | | NR |
| Crompton et al. 2017 | 39; 0; 0; 0 | 3,426 | Critically low | RR: 0.82 (0.70-0.96) | | I2=49% |  | | NR |
| Leng et al. 2017 | 7; 0; 0; 0 | 1,331 | Critically low | OR: 1.21 (0.93-1.57) | | I2=46% |  | | NR |
| Zang et al. 2017 | 19; 0; 0; 0 | 2,245 | Critically low | RR: 0.78 (0.64-0.96) | | I2=44% |  | | NR |
| Olah et al. 2018  *All studies*  *High quality* | 14; 0; 0; 0  3; 0; 0; 0 | NR  NR | High | OR: 0.68 (0.52-0.88)  OR: 0.79 (0.38-1.63) | | NR  NR |  | | NR |
| Watson et al. 2018  *All studies*  *High quality* | 21; 0; 0; 0  2; 0; 0; 0 | 2,330  552 | Low | RR: 0.83 (0.73-0.94)  RR: 1.37 (1.04-1.79) | | I2=45%  I2=0% |  | | NR |
| Pneumonia | | | | | | | | | |
| Harris et al. 2002 | 3; 0; 0; 0 | 136 | Critically low | OR: 2.05 (0.79-5.32) | | P=0.24 |  | | NR |
| Henderson et al. 2003 | 5; 0; 0; 0 | 272 | Critically low | OR: 0.42 (0.25-0.70) | | NR |  | | NR |
| Sydenham et al. 2009 | 10; 0; 0; 0 | 322 | Low | OR: 2.06 (1.28-3.30) | | I2=30% |  | | NR |
| Crossley et al. 2014 | 12; 0; 0; 0 | 689 | High | RR: 0.81 (0.62-1.05) | | I2=46% |  | | NR |
| Zhu et al. 2016 | 13; 0; 0; 0 | 844 | Moderate | RR: 1.51 (1.12-2.03) | | I2=55% |  | | NR |
| Crompton et al. 2017 | NR | NR | Critically low | RR: 1.28 (1.01-1.62) | | NR |  | | NR |
| Watson et al. 2018 | 14; 0; 0; 0 | 1,188 | Low | RR: 1.50 (1.23-1.83) | | I2=0% |  | | NR |
| **Decompressive craniectomy in adults with traumatic brain injury** | | | | | | | | | |
| Mortality | | | | | | | | | |
| Wang et al. 2016 | 2; 0; 0; 0 | 175 | Critically low | RR: 0.92 (0.50-1.71) | | I2=6% | Low: 1/2 | | NR |
| Zhang et al. 2017 | 4; 0; 0; 0 | 645 | Critically low | RR: 0.59 (0.47-0.74) | | I2=20% | Low: 2/4 | | NR |
| Tsaousi et al. 2018 | 3; 0; 0; 0 | 564 | Critically low | RR: 0.61 (0.47-0.78) | | I2=43% | Low: 0/3 | | NR |
| Lu et al. 2018 | 4; 0; 0; 0 | 622 | Critically low | OR: 0.46 (0.33-0.64) | | I2=47% | Low: 0/4 | | NR |
| Length of stay | | | | | | | | | |
| Zhang et al. 2017 | 2; 0; 0; 0 | 182 | Critically low | MD: -4.63 (-6.62 to -2.65) | | I2=0% | Low: 2/4 | | NR |
| Lu et al. 2019 | 2; 0; 0; 0 | 182 | Critically low | MD: -13.81 (-25.26 to -2.37) | | I2=78% | Low: 0/4 | | NR |
| Complications | | | | | | | | | |
| Zhang et al. 2017 | 2; 0; 0; 0 | 92 | Critically low | RR: 1.94 (1.31-2.87) | | I2=0% | Low: 2/4 | | NR |
| Lu et al. 2019 | 2; 0; 0; 0 | 229 | Critically low | OR: 3.85 (1.36-10.92) | | I2=0% | Low: 0/4 | | NR |
| Intracranial pressure | | | | | | | | | |
| Zhang et al. 2017 | 4; 0; 0; 0 | 581 | Critically low | MD: -2.12 (-2.81 to -1.43) | | I2=77.8% | Low: 2/4 | | NR |
| Lu et al. 2019 | 3; 0; 0; 0 | 627 | Critically low | MD: -3.59 (-4.94 to -2.23) | | I2=81% | Low: 0/4 | | NR |

AMSTAR, Assessing the Methodological Quality of Systematic Reviews; CCHR, Canadian CT Head Rule; CHIP, CT in Head Injury Patients; CI, confidence intervals; CT, computed tomography; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, mean difference; NA, not applicable; NEXUS-II, the National Emergency X-Radiography Utilisation Study II; NR, not reported; OR, odds ratio; P, proportion; RR, relative risks; RCT, randomized controlled trials; TBI, traumatic brain injury

\*False omission rate, calculated as «1 – negative predictive value (i.e., true negatives / [true negatives + false negatives])»

Interpretation of AMSTAR-2: High: no or one non-critical weakness, Moderate: more than one non-critical weakness, Low: one critical flaw with or without non-critical weaknesses, Critically low: more than one critical flaw with or without non-critical weaknesses