Table 3. Synthesis of results for therapeutic interventions

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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 primary outcome**  **(95% CI)** | **Heterogeneity**  χ2, **Q or I2** | **Reported risk of bias in original studies** | **Reported GRADE** |
| **Platelet transfusion in adults with acute traumatic brain injury on antiplatelet therapy** | | | | | | | |
| Mortality | | | | | | | |
| Nishijima et al. 2012 | 0; 0; 5; 0 | 635  (34 to 195) | Critically low | OR: 0.21 (0.05-0.95) to  2.42 (1.18-4.96) | NA | NR | Low to  very low |
| Kumar et al. 2015  *With thrombocytopenia*  *Without thrombocytopenia* | 0; 0; 5; 0  0; 0; 1; 0 | 804  108 | Moderate | OR: 1.55 (0.75-3.18)  OR: 7.59 (0.36-161.99) | I2=68%  NA | Low: 0/5  Low: 0/1 | Very low  Very low |
| Leong et al. 2015 | 0; 0; 4; 0 | 711 | Critically low | OR: 1.77 (1.00-3.13) | I2=36% | #studies ≥ 70% items  6/7 | NR |
| **Antibiotic prophylaxis in adults with basal skull fractures** | | | | | | | |
| Meningitis | | | | | | | |
| Ratilal et al. 2015  *With CSF leakage*  *Without CSF leakage* | 3; 0; 0; 0  2; 0; 0; 0 | 92  106 | Moderate | OR: 0.44 (0.09-2.15)  OR: 0.77 (0.25-2.41) | I2=0%  NR | #studies ≥ 70% items  2/3  1/2 | Moderate |
| **Antibiotic prophylaxis for external ventricular drain placement in adults with acute traumatic brain injury** | | | | | | | |
| Infections | | | | | | | |
| Ratilal et al. 2010 | 1; 0; 0; 0 | 52 | High | OR: 1.08 (0.06-18.30) | NA | Unclear risk of bias | NR |
| **Extended seizure prophylaxis >1 week in adults with severe TBI** | | | | | | | |
| Late seizures‡ | | | | | | | |
| Temkin et al. 2001  *Carbamazepine*  *Phenobarbital*  *Phenobarbital+Phenytoin*  *Phenytoin*  *Valproate* | 1; 0; 0; 0  1; 0; 0; 0  1; 0; 0; 0  4; 0; 0; 0  1; 0; 0; 0 | 110  163  148  812  344 | Critically low | RR: 0.70 (0.33-1.50)  RR: 0.45 (0.12-1.73)  RR: 0.36 (0.08-1.73)  RR: 1.08 (0.76-1.55)  RR: 1.28 (0.76-2.16) | NR  NR  NR  NR  NR | NR | NR |
| Chang et al. 2003  *Carbamazepine, phenytoin and valproate combined* | 5; 0; 0; 0 | 1,312 | Critically low | RR: 1.05 (0.82-1.35) | NR | Low, moderate: 5/5 | NR |
| Thompson et al. 2015  *Carbamazepine and phenytoin combined* | 6; 0; 0; 0 | 1,029 | Moderate | RR: 0.91 (0.57-1.47) | I2=54% | #studies ≥ 70% items  2/7 | Very low |
| Wilson et al. 2018  *Levetiracetam*  *Phenytoin* | 2; 0; 0; 0  3; 0; 1; 0 | 164  716 | Critically low | OR: 0.69 (0.24-1.96)  OR: 0.40 (0.10-1.60) | NR  NR | Low: 2/2  Low: 4/4 | High  High |
| **Therapeutic hypothermia in adults with acute traumatic brain injury** | | | | | | | |
| GOS or GOS-E – unfavorable outcome | | | | | | | |
| Harris et al. 2002 | 4; 0; 0; 0 | 499 | Critically low | OR: 0.61 (0.26-1.46) | χ2: 6.87 (p=0.08) | 0/7 | NR |
| Henderson et al. 2003 | 8; 0; 0; 0 | 748 | Critically low | OR: 0.75 (0.56-1.10) | χ2: 16.56 (p=0.02) | Low: 3/8 | NR |
| McIntyre et al. 2003 | 10; 0; 0; 0 | 779 | Low | RR: 0.78 (0.63-0.98) | Q=16.05 | Low, moderate: 5/10 | NR |
| Bratton et al. 2007 | 6; 0; 0; 0 | 694 | Critically low | RR: 0.68 (0.52-0.89) | I2=47.5% | Low, moderate: 6/6¥ | NR |
| Peterson et al. 2008 | 12; 0; 0; 0 | 1,294 | Low | RR: 0.73 (0.59-0.90) | I2=57.8% | Low: 1/12 | NR |
| Sydenham et al. 2009  *All studies*  *High quality studies* | 20; 0; 0; 0  8; 0; 0; 0 | 1,382  686 | Low | OR: 0.69 (0.55-0.86)  OR: 0.79 (0.57-1.08) | I2=38%  I2=0% | Low: 8/20 | NR |
| Fox et al. 2010 | 10; 0; 0; 0 | 1,223 | Moderate | RR: 0.66 (0.56-0.78) | I2=34.1% | Low: 7/10 |  |
| Georgiou et al. 2013  *All studies*  *High quality studies* | 18; 0; 0; 0  3; 0; 0; 0 | 1,733  670 | Low | RR: 0.81 (0.73-0.89)  RR: 1.07 (0.92-1.24) | I2=63%  I2=1% | Low, moderate: 5/18 | Low |
| Crossley et al. 2014  *All studies*  *High quality studies* | 20; 0; 0; 0  16; 0; 0; 0 | 1,885  964 | High | RR: 0.67 (0.78-0.57)  RR: 0.60 (0.52-0.69) | I2=51%  I2=0% | Low: 16/20 | NR |
| Li et al. 2014 | 10; 1; 0; 0 | 1,029 | Critically low | RR: 0.83 (0.65-1.05) | I2=61% | NR | NR |
| Zhu et al. 2016  *All studies*  *High quality studies* | 11; 0; 0; 0  5; 0; 0; 0 | 1,651  781 | Moderate | RR: 0.80 (0.63-1.00)  RR: 0.84 (0.62-1.15) | I2=78%  I2=76% | Low: 5/11 | NR |
| Crompton et al. 2017 | 20; 14; 1; 0 | 3,109 | Critically low | RR: 0.74 (0.65-0.85) | I2=53% | NR | NR |
| Leng et al. 2017 | 7; 0; 0; 0 | 1,324 | Critically low | OR: 1.00 (0.79-1.21) | I2=68% | NR | NR |
| Zang et al. 2017 | 21; 0; 0; 0 | 2,302 | Critically low | RR: 0.71 (0.60-0.84) | I2=72% | Low: 10/21 | NR |
| Watson et al. 2018  *All studies*  *High quality studies* | 22; 0; 0; 0  2; 0; 0; 0 | 2,346  522 | Low | RR: 0.81 (0.75-0.87)  RR: 1.16 (1.02-1.32) | I2=71%  I2=0% | Low: 2/22 | NR |
| **Decompressive craniectomy in adults with traumatic brain injury** | | | | | | | |
| GOS/GOS-E – unfavorable outcome | | | | | | | |
| Wang et al. 2016 | 2; 0; 0; 0 | 175 | Critically low | RR: 0.89 (0.34-2.37) | I2=81% | Low: 1/2 | NR |
| Zhang et al. 2017 | 4; 0; 0; 0 | 645 | Critically low | RR: 0.85 (0.61-1.18) | I2=73% | Low: 2/4 | NR |
| Tsaousi et al. 2018 | 3; 0; 0; 0 | 564 | Critically low | RR: 0.94 (0.63-1.41) | I2=75% | Moderate: 1/3 | NR |
| Lu et al. 2019 | 4; 0; 0; 0 | 622 | Critically low | OR: 0.75 (0.32-1.75) | I2=77% | Low: 0/4 | NR |

AMSTAR, Assessing the Methodological Quality of Systematic Reviews; CI, confidence intervals; CSF, cerebrospinal fluid; CT, computed tomography; GOS-E, Glasgow Outcome Scale-Extended; GRADE, Grading of Recommendations Assessment, Development and Evaluation; 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

†AMSTAR-2 interpretations: 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 weaknessess

†Antiepileptic drugs were compared to either placebo, no treatment or other pharmacologic agents

¥Seven RCTs at high risk of bias were excluded