Table 1. Characteristics of included systematic reviews according to PICOS

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **First author**  **publication year**  **type of review** | **Date last search** | **Population** | **Intervention** | **Comparator** | **Primary outcomes** | **Secondary outcomes** | **Study designs** |
| **Head computed tomography** | | | | | | | |
| **Pandor 2011**  *Systematic review* | March 2010 | Adults with mild head injury (GCS 13-15) | CDR (head CT) | None | Intracranial abnormality  Neurosurgical intervention | NR | Diagnostic cohort (P/R) |
| **Easter 2015**  *Systematic review* | August 2015 | Adults with mild head injury (GCS 13-15) | CDR (head CT) | None | Severe intracranial injury | Mortality  Neurosurgical intervention | NR |
| **Repeat head computed tomography** | | | | | | | |
| **Stippler 2012**  *Systematic review* | February 2011 | Mild complicated TBI (GCS 13-15 with abnormal initial CT finding) | Repeat CT | NR  (no repeat CT) | Neurosurgical intervention  Progression of injury | NR | NR |
| **Almenawer 2013**  *Meta-analysis* | February 2012 | Mild head injury | Repeat CT | NR  (no repeat CT) | Neurological deterioration  Neurosurgical intervention  Progression of injury | NR | NR |
| **Reljic 2014**  *Meta-analysis* | February 2012 | TBI | Repeat CT | NR  (no repeat CT) | Change in clinical management | ICP monitoring  Neurosurgical intervention  Progression of injury | RCT  Cohort (P/R)  Cross-sectional  Case-control |
| **Chauny 2016**  *Meta-analysis* | September 2015 | Mild TBI with normal initial CT, on pre-injury vitamin K antagonist | Repeat CT (<24h) | NR  (no repeat CT) | Delayed intracranial hemorrhage ≤24h | Mortality  Neurosurgical intervention | RCT  Cohort (P/R)  Cross-sectional  Case-control |
| **Marincowitz 2018**  *Meta-analysis* | 2016 | Mild complicated TBI (≥12yo; GCS 13-15 with abnormal initial CT finding) | Repeat CT | NR  (no repeat CT) | Clinical deterioration  Mortality  Neurosurgical intervention | Progression of injury | All designs other than case studies |
| **Plasma transfusion** | | | | | | | |
| **Yang 2012**  *Systematic review* | July 2011 | Hospitalisations <3h of severe closed head injury | Frozen plasma transfusion | NR | Mortality | Blood loss  Coagulation test abnormalities  LOS  Side effects | RCT |
| **Platelet transfusion** | | | | | | | |
| **Nishijima 2012**  *Systematic review* | August 2011 | Adult traumatic ICH with pre-injury oral anti-platelet use | Transfusion of platelets at any dose, within 24 hours | No platelet transfusion | GOS-E  Mortality | Infection  Transfusion reaction Transfusion-  related lung injury | RCT  Observational |
| **Kumar 2015**  *Meta-analysis* | September 2014 | Patients with TBI | Apheresis or whole-blood derived platelet transfusion concentrates (therapeutic or prophylactic) | No platelet transfusion | All-cause mortality | Bleeding-related mortality  Number of platelet transfusions | RCT  Cohort (P/R)  Case-control |
| **Leong 2015**  *Meta-analysis* | June 2014 | Adult traumatic ICH with pre-injury antiplatelet use | Platelet transfusion | No platelet transfusion | In-hospital mortality | Acute clinical deterioration  Chronic clinical  Delayed mortality  LOS | RCT  Cohort (P/R)  Case-control |
| **Antibiotic prophylaxis** | | | | | | | |
| **Ratilal 2010**  *Meta-analysis* | 2010 | Patients with intracranial ventricular cerebrospinal fluid shunt | Prophylactic antibiotics | Placebo or standard treatment | Adverse events  Mortality  Shunt infection  Shunt revision | Cognitive function  Disability  LOS  Quality of life | RCT  Quasi-randomised |
| **Ratilal 2015**  *Meta-analysis* | June 2014 | Basilar skull fracture | Prophylactic antibiotics | Placebo or no intervention | Meningitis | All-cause mortality  Meningitis-related mortality  Surgical correction for CSF leakage  Non-CNS infection | RCT |
| **Antiseizure prophylaxis** | | | | | | | |
| **Temkin 2001**  *Meta-analysis* | NR | TBI | Antiepileptic drug | Placebo, no treatment, or drug that does not influence the seizure rate | Early PTS | Early and late PTS | NR |
| **Chang 2003**  *Meta-analysis* | November 2001 | Severe TBI | Antiepileptic drug prophylaxis | Placebo or other | Early and late PTS | NR | RCT  Quasi-randomized  Cohort (P) |
| **Teasell 2007**  *Systematic review* | 2005 | Moderate to severe TBI | Prophylactic anticonvulsants | NR | Early and late PTS | NR | NR |
| **Thompson 2015**  *Meta-analysis* | September 2014 | TBI | Antiepileptic drug or alternative pharmacologic treatments | Placebo, usual care or other pharmacologic agents | Early and late PTS | Adverse events  Mortality  Time to first seizure | RCT |
| **Wilson 2018**  *Meta-analysis* | May 2016 | TBI | Antiepileptic drug | Placebo or another PTS prophylaxis | Early and late PTS | NR | NR |
| **Neuromuscular blocking agents (NMBAs)** | | | | | | | |
| **Sanfilippo 2015**  *Systematic review* | January 2014 | Adult TBI and/or raised ICP | NMBAs (bolus or continuous infusion) | Same patient or control | Cardiovascular parameters  ICP  Morbidity  Respiratory parameters | NR | RCT  Cohort (P/R)  Case series (>5patients) |
| **Hypothermia** | | | | | | | |
| **Harris 2002**  *Meta-analysis* | NR | TBI (≥10yo) | Hypothermia (32-35 °C) | Normothermia | Arrhythmia  GOS  ICP  Partial thromboplastin time  Pneumonia  Prothrombin time | NR | RCT |
| **Henderson 2003**  *Meta-analysis* | 2002 | TBI | Hypothermia (32-35 °C) | NR | Mortality | GOS  Pneumonia | RCT |
| **McIntyre 2003**  *Meta-analysis* | September 2002 | Adult TBI | Hypothermia (30-35 °C) ≥24 hr | Normothermia | Mortality | GOS | RCT |
| **Bratton 2007**  *Meta-analysis* | April 2006 | Patients (≥14yo) with TBI | Hypothermia regardless of ICP  (32-35 °C) | Normothermia | Mortality | GOS | RCT |
| **Peterson 2008**  *Meta-analysis* | June 2007 | Adults with TBI | Hypothermia  (30-35 °C) | Standard of care | Mortality | Arrhythmia  GOS  Pneumonia | RCT |
| **Sydenham 2009**  *Meta-analysis* | May 2008 | Patients with closed traumatic head injury requiring hospitalisation | Hypothermia (30-35 °C) ≥12 hr | Standard of care | Mortality  GOS | Pneumonia | RCT |
| **Fox 2010**  *Meta-analysis* | NR | Adult severe TBI (GCS≤8) without major contraindications | Hypothermia (32-35 °C) | Standard of care | GOS  Mortality | NR | RCT |
| **Lu 2012**  *Systematic review* | June 2011 | Adult TBI | Hypothermia  (32-35 °C) | NR | Mortality  GOS  Quality of life  Recovery | NR | RCT |
| **Georgiou 2013**  *Meta-analysis* | July 2011 | TBI | Hypothermia  (30-35 °C) ≥12 hr | NR | GOS  Survival | NR | RCT |
| **Crossley 2014**  *Meta-analysis* | January 2012 | Adults with closed head injuries | Hypothermia  (32-35 °C) | Normothermia | Mortality  GOS  Pneumonia | NR | RCT |
| **Li 2014**  *Meta-analysis* | December 2012 | Severe TBI | Hypothermia  (32-35 °C) | Normothermia | GOS  Mortality | NR | RCT  Cohort (P/R)  Cross-sectional |
| **Saxena 2014**  *Systematic review* | September 2013 | TBI | Any physical or drug therapy that reduces temperature to no less than 35°C | NR | GOS  Mortality | Abnormal ICP  Mortality  Extracranial haemorrhage  Neurosurgical intervention  Pneumonia or other serious infections | RCT |
| **Zhu 2016**  *Meta-analysis* | NR | Adult TBI | Hypothermia (32-35°C) | Normothermia | GOS  Mortality | Complications (bleeding, cardiovascular, pneumonia) | RCT |
| **Crompton 2017**  *Meta-analysis* | February 2016 | TBI | Hypothermia  (30-35 °C) | No temperature management (except for fever control) | Arrhythmia  Mortality  Pneumonia | GOS | RCT  Observational |
| **Dunkley 2017**  *Systematic review* | NR | Adult severe TBI | Hypothermia  (33-35 °C) | Normothermia | GOS | Complications  Abnormal ICP | NR |
| **Leng 2017**  *Meta-analysis* | NR | TBI without major contraindications | Hypothermia (32-36°C) in addition to standard of care | Standard of care | GOS Mortality | NR | NR |
| **Zang 2017**  *Meta-analysis* | June 2016 | Adult TBI | Hypothermia (32-35 °C) | NR | Mortality | GOS or GOS-E | RCT |
| **Olah 2018**  *Meta-analysis* | February 2017 | Adult severe TBI | Hypothermia (32-35 °C) | No cooling | Mortality | NR | RCT  Quasi-randomized  Observational |
| **Watson 2018**  *Meta-analysis* | January 2018 | Adult moderate or severe (GCS ≤12) closed head injury | Hypothermia (32-35°C) | Control (normothermia and other) | GOS  Mortality  Pneumonia | NR | NR |
| **Decompressive craniectomy** | | | | | | | |
| **Barthelemy 2016**  *Meta-analysis* | April 2015 | Adult closed severe TBI (GCS<8) | Decompressive craniectomy | NR | GOS  Mortality | ICP,  Quality of life | RCT  Observational  Case series |
| **Wang 2016**  *Meta-analysis* | July 2014 | Severe TBI (confirmed by CT or MRI) with refractory ICP | Decompressive craniectomy | Conservative treatment | GOS or GOS-E | Mortality | RCT |
| **Abraham 2017**  *Systematic review* | May 2017 | Severe TBI | Decompressive craniectomy | NR | NR | NR | RCT |
| **Zhang 2017**  *Meta-analysis* | October 2016 | TBI | Decompressive craniectomy | Medical therapies | Mortality | Complications  GOS  ICP  LOS  ICU LOS | RCT |
| **Tsaousi 2018**  *Meta-analysis* | April 2017 | TBI with refractory intracranial hypertension | Decompressive craniectomy | Standard of care | GOS  Mortality | Adverse events  ICP  ICU LOS  Time to discharge | RCT  Observational  Case series |
| **Lu 2019**  *Meta-analysis* | June 2016 | TBI | Decompressive craniectomy | Standard of care | GOS  Mortality | Adverse events  ICP  LOS | RCT |

CDR, clinical decision rule; ED, emergency department; GCS, Glasgow Coma Scale; GOS-E, Glasgow Outcome Scale – Extended; ICH, intracranial hemorrhage; ICP, intracranial pressure; LOS, length of stay; NMBAs, neuromuscular blocking agents; NR, not reported; P, prospective; PTS, post-traumatic seizure; R, retrospective; RCT, randomized controlled trial; yo, years old