# Appendix A: Summary of evidence from surveillance

## 2017 surveillance – Head injury (2014) NICE guideline CG176



## Summary of evidence from surveillance

### *Terms used in this guideline*

**Focal neurological deficit**

Problems restricted to a particular part of the body or a particular activity, for example, difficulties with understanding, speaking, reading or writing; decreased sensation; loss of balance; general weakness; visual changes; abnormal reflexes; and problems walking.

**High-energy head injury**

For example, pedestrian struck by motor vehicle, occupant ejected from motor vehicle, fall from a height of greater than 1 metre or more than 5 stairs, diving accident, high-speed motor vehicle collision, rollover motor accident, accident involving motorised recreational vehicles, bicycle collision, or any other potentially high-energy mechanism.

**Base of open or depressed skull fracture or penetrating head injury**

Signs include clear fluid running from the ears or nose, black eye with no associated damage around the eyes, bleeding from one or both ears, bruising behind one or both ears, penetrating injury signs, visible trauma to the scalp or skull of concern to the professional.

The wording used in the recommendations in this guideline (for example words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See About this guideline for details.

### *Pre-hospital assessment, advice and referral to hospital*

**176 – 01 Pre-hospital assessment, advice and referral to hospital**

#### Recommendations derived from this review question

*General advice*

1.1.1 Public health literature and other non-medical sources of advice (for example, St John Ambulance, police officers) should encourage people who have any concerns following a head injury to themselves or to another person, regardless of the injury severity, to seek immediate medical advice. [2003]

*Telephone advice services*

1.1.2 Telephone advice services (for example, NHS 111, emergency department helplines) should refer patients who have sustained a head injury to the emergency ambulance services (that is, 999) for emergency transport to the emergency department if they have experienced any of the following:

- Unconsciousness or lack of full consciousness (for example, problems keeping eyes open).
- Any focal neurological deficit since the injury.
- Any suspicion of a skull fracture or penetrating head injury.
- Any seizure ('convulsion' or 'fit') since the injury.
- A high-energy head injury.
- The injured person or their carer is incapable of transporting the injured person safely to the hospital emergency department without the use of ambulance services (providing any other risk factor indicating emergency department referral is present; see recommendation 1.1.3). [2003, amended 2007 and 2014]

1.1.3 Telephone advice services (for example, NHS 111 or emergency department helplines) should refer patients who have sustained a head injury to a hospital emergency department if they have any of the following risk factors:

- Any loss of consciousness ('knocked out') as a result of the injury, from which the person has now recovered.
- Amnesia for events before or after the injury ('problems with memory')*.
- Persistent headache since the injury.
- Any vomiting episodes since the injury.
- Any previous brain surgery.
- Any history of bleeding or clotting disorders.
- Current anticoagulant therapy such as warfarin.
- Current drug or alcohol intoxication.
- There are any safeguarding concerns (for example, possible non-accidental injury or a vulnerable person is affected).
- Irritability or altered behaviour ('easily distracted', 'not themselves', 'no concentration', 'no interest in things around them'), particularly in infants and children aged under 5 years.
- Continuing concern by helpline staff about the diagnosis. [2003, amended 2014]

### *Community health services and NHS minor injury clinics*

1.1.4 Community health services (GPs, ambulance crews, NHS walk-in centres, dental practitioners) and NHS minor injury clinics should refer patients who have sustained a head injury to a hospital emergency department, using the ambulance service if deemed necessary, if any of the following are present:

- Glasgow coma scale (GCS) score of less than 15 on initial assessment.
- Any loss of consciousness as a result of the injury.
- Any focal neurological deficit since the injury.
- Any suspicion of a skull fracture or penetrating head injury since the injury.
- Amnesia for events before or after the injury.*
- Persistent headache since the injury.
- Any vomiting episodes since the injury (clinical judgement should be used regarding the cause of vomiting in those aged 12 years or younger and the need for referral).
- Any seizure since the injury.
- Any previous brain surgery.
- A high-energy head injury.
- Any history of bleeding or clotting disorders.
- Current anticoagulant therapy such as warfarin.

- Current drug or alcohol intoxication.
- There are any safeguarding concerns (for example, possible non-accidental injury or a vulnerable person is affected).
- Continuing concern by the professional about the diagnosis. [2003, amended 2007 and 2014].

* Assessment of amnesia will not be possible in preverbal children and is unlikely to be possible in children aged under 5 years.

1.1.5 In the absence of any risk factors in recommendation 1.1.4, consider referral to an emergency department if any of the following factors are present, depending on judgement of severity:

- Irritability or altered behaviour, particularly in infants and children aged under 5 years.
- Visible trauma to the head not covered in recommendation 1.1.4 but still of concern to the professional.
- No one is able to observe the injured person at home.
- Continuing concern by the injured person or their family or carer about the diagnosis. [2003, amended 2014]

### *Transport to hospital from community health services and NHS minor injury clinics*

1.1.6 Patients referred from community health services and NHS minor injury clinics should be accompanied by a competent adult during transport to the emergency department. [2003]

1.1.7 The referring professional should determine if an ambulance is required, based on the patient's clinical condition. If an ambulance is deemed not required, public transport and car are appropriate means of transport providing the patient is accompanied. [2003]

1.1.8 The referring professional should inform the destination hospital (by phone) of the impending transfer and in non-emergencies a letter summarising signs and symptoms should be sent with the patient. [2003]

### *Training in risk assessment*

1.1.9 GPs, nurse practitioners, dentists and ambulance crews should receive training, as necessary, to ensure that they are capable of assessing the presence or absence of the risk factors listed in recommendations 1.1.4 and 1.1.5. [2003, amended 2007]

## Surveillance decision

This review question should not be updated.

---

### *Risk factors for brain injury in children*

**Surveillance summary (2017)**

A cross-sectional study[1] included 1,775 children with head injury resulting from a fall. Isolated skull fracture was seen in 16.9% of the study population and intracranial injury occurred in 13.7%. However, 12% of children with GCS 15, or alert, had intracranial injury. Compared with falls from standing, the likelihood of intracranial injury was higher for falls from a person's arms, from an 'infant or child product' or from a building attic or window.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

The definition of high-energy head injury may not fully capture risk of head injury in children. However, expanding the definition is not likely to be urgent because it relates only to advice on referral for ambulance transport. Children with non-high-energy head injuries should receive medical assessment under current recommendations.

New evidence is unlikely to change guideline recommendations.

### *Head injury in people with renal disease*

**Surveillance summary (2017)**

An analysis[2] of national registry data from Taiwan included 6,938 people on haemodialysis for end-stage renal disease who had head injury compared with 13,876 randomly selected controls who were not receiving haemodialysis. After adjustment for age, gender and other pre-existing conditions, people undergoing haemodialysis had no greater risk of intracranial haemorrhage after head injury than controls. Immediate intracranial haemorrhage was significantly lower in the haemodialysis group.

**Topic expert feedback**

Topic expert feedback suggested that people with renal disease who had uraemia or are on dialysis may have a greater likelihood of haemorrhage after head injury.

**Impact statement**

The guideline does not include renal disease as a specific risk factor for haemorrhage after head injury. We did not find evidence to support updating the guideline to include renal disease as a significant risk factor for intracranial haemorrhage after head injury at this time.

New evidence is unlikely to change guideline recommendations.

### *Bathroom injuries*

**Surveillance summary (2017)**

A cross-sectional analysis[3] included 280 people presenting to an emergency department who had accidents involving showers or bathtubs. Traumatic brain injury was identified in 10% of the sample. In univariate analysis, intracranial haemorrhage was associated with direct trauma, increased age, but not with the mechanism or location of the fall compared with controls who had traumatic brain injury but no intracranial haemorrhage. Multivariate analysis suggested that age was the only significant risk factor for intracranial haemorrhage.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Evidence suggests that intracranial haemorrhage may occur after bathroom falls. However, the lack of comparison against control, such as non-bathroom falls from standing means this evidence cannot determine whether bathroom falls are a particular risk factor for head injury to guide referral to medical services.

New evidence is unlikely to change guideline recommendations.

## *Immediate management at the scene and transport to hospital*

**176 – 02 The benefits of direct transport from the scene to a specialist neurosciences centre compared to transport to the nearest district general hospital**

### Recommendations derived from this review question

*Glasgow coma scale*

1.2.1 Base monitoring and exchange of information about individual patients on the three separate responses on the GCS (for example, a patient scoring 13 based on scores of 4 on eye-opening, 4 on verbal response and 5 on motor response should be communicated as E4, V4, M5). [2003]

1.2.2 If a total score is recorded or communicated, base it on a sum of 15, and to avoid confusion specify this denominator (for example, 13/15). [2003]

1.2.3 Describe the individual components of the GCS in all communications and every note and ensure that they always accompany the total score. [2003]

1.2.4 In the paediatric version of the GCS, include a 'grimace' alternative to the verbal score to facilitate scoring in preverbal children. [2003]

1.2.5 In some patients (for example, patients with dementia, underlying chronic neurological disorders or learning disabilities) the pre-injury baseline GCS may be less than 15. Establish this where possible, and take it into account during assessment. [new 2014]

*Initial assessment and care*

1.2.6 Initially assess adults who have sustained a head injury and manage their care according to clear principles and standard practice, as embodied in the:

- Advanced Trauma Life Support (ATLS) course/European Trauma course.
- International Trauma Life Support (ITLS) course.
- Pre-hospital Trauma Life Support (PHTLS) course.
- Advanced Trauma Nurse Course (ATNC).
- Trauma Nursing Core Course (TNCC).
- Joint Royal Colleges Ambulance Service Liaison Committee (JRCALC) Clinical Practice Guidelines for Head Trauma. [2003, amended 2007]

1.2.7 Initially assess children who have sustained a head injury and manage their care according to clear principles outlined in the:

- Advanced Paediatric Life Support (APLS)/European Paediatric Life Support (EPLS) course.
- Pre-hospital Paediatric Life Support (PHPLS) course.
- Paediatric Education for Pre-hospital Professionals (PEPP) course. [2003, amended 2007]

1.2.8 When administering immediate care, treat first the greatest threat to life and avoid further harm. [2003]

1.2.9 Attempt full cervical spine immobilisation for patients who have sustained a head injury and present with any of the following risk factors unless other factors prevent this:

- GCS less than 15 on initial assessment by the healthcare professional.
- Neck pain or tenderness.
- Focal neurological deficit.
- Paraesthesia in the extremities.

- Any other clinical suspicion of cervical spine injury. [2003, amended 2007]

1.2.10 Maintain cervical spine immobilisation until full risk assessment including clinical assessment (and imaging if deemed necessary) indicates it is safe to remove the immobilisation device. [2003, amended 2007]

1.2.11 Make standby calls to the destination emergency department for all patients with GCS 8 or less to ensure appropriately experienced professionals are available for their treatment and to prepare for imaging. [2003]

1.2.12 Manage pain effectively because it can lead to a rise in intracranial pressure. Provide reassurance, splintage of limb fractures and catheterisation of a full bladder, where needed. [2007, amended 2014]

1.2.13 Follow at all times best practice in paediatric coma observation and recording as detailed by the National Paediatric Neuroscience Benchmarking Group. [2003]

## Surveillance decision

This review question should not be updated.

An editorial correction is needed to include a cross-reference in recommendation 1.2.8 to the more recent guideline on major trauma (NICE NG39), which has recommendations on volume resuscitation in people with traumatic brain injury and haemorrhagic shock.

---

### *Pain management*

**Surveillance summary (2017)**

A cohort study[4] (number of participants not reported in the abstract) included people with minor head injury who received intravenous morphine before undergoing CT. In people aged 15–60 years, response to morphine was associated with normal CT findings with a sensitivity of 100%. However, in people older than 60 years, the association was less clear, with sensitivity of 58% for normal CT findings and 71% for neurosurgical intervention.

A randomised controlled trial[5] (RCT; n=60) assessed intravenous paracetamol compared with intravenous morphine in adults (18–55 years) with headache (more than 40 mm on a 100 mm visual analogue scale) due to head trauma. The dosage of each drug was not reported in the abstract. In the paracetamol group, after 30 minutes headache was reduced to a significantly greater extent than in the morphine group. No participants had pathological findings on clinical examination or imaging.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Evidence suggests that pain from head injury without brain injury may be managed effectively with intravenous paracetamol. Additionally, non-response to morphine may be a sign of clinically significant brain injury. These findings provide support for the recommendation to manage pain effectively.

New evidence is unlikely to change guideline recommendations.

---

### *Resuscitation fluid*

**Surveillance summary (2017)**

An analysis[6] assessed data (n=791) from the PROMMTT (PRospective Observational Multicenter Major Trauma Transfusion) study of pre-hospital administration of lactated Ringer's solution compared with normal saline in people with trauma (with or without head injury). People who received lactated Ringer's solution had worse injury scores than those receiving normal saline. In people with traumatic brain injury, lactated Ringer's solution was associated with greater adjusted mortality than normal saline. However, this effect was not seen in people without brain injuries.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Current guidance does not make recommendations on types of fluid used for resuscitation. NICE guidance on assessment and initial management of major trauma (NG39) has further recommendations in this area. However, evidence suggests no role for lactated Ringer's solution in immediate management of people with head trauma.

New evidence is unlikely to change guideline recommendations.

---

### *Prehospital airway management*

**Surveillance summary (2017)**

A systematic review and meta-analysis[7] of 6 studies (n=4,772) assessed prehospital intubation compared with non-invasive airway management in adults with severe traumatic brain injury. Mortality was significantly higher in people who had intubation by inexperienced emergency staff, whereas there was no significant association with mortality when intubation was performed by emergency staff with 'extended level' training.

A retrospective cohort study[8] included 55 people with isolated traumatic brain injury who received prehospital intubation and 165 controls who had oxygen delivered by a mask only. Cases and controls were matched by demographics, mechanism of injury, presence of tachycardia or hypotension, Injury Severity Score, type of intracranial lesion, and all major surgical interventions. Prehospital intubation was associated with significantly higher mortality than oxygen masks. The intubation group also had significantly lower $pO_2$ at admission and significantly higher incidence of septic shock.

A cohort study[9] included 124 people admitted with severe traumatic brain injury. Prehospital airway management was analysed, with basic airway management being associated with increased likelihood of a good outcome than people who had prehospital intubation. People intubated without drugs had the worst outcome, followed by rapid sequence intubation, and then sedation-assisted intubation.

An analysis[10] of data from the Resuscitation Outcomes Consortium out-of-hospital clinical trial included 1,239 people with traumatic brain injury and 778 people with shock. An 'out-of-hospital' time of more than 60 minutes was not associated with worse outcomes in either the shock group or the traumatic brain injury group after adjustment for important confounding factors. A further analysis from this study[11] included 1,116 people with traumatic brain injury and 528 people with haemorrhagic shock. The analysis excluded people who died at the scene and those with missing data on advanced airway management. After adjustment for confounding factors, out-of-hospital advanced airway management was associated with significantly poorer neurological outcome at 6 months, but there was no evidence of an effect on 28-day mortality or 6-month functional outcome.

A retrospective cohort study[12] included children aged under 18 years with severe traumatic brain injury who were intubated for at least 48 hours. The number of children included in analysis was not reported in the abstract. Adherence to US guidelines for managing severe head trauma in children was assessed. Clinical indicators of adherence to guidelines were associated with increased survival. In particular, absence of prehospital hypoxia, early start of nutrition in intensive care units, and absence of clinical or radiographic signs of cerebral herniation. Favourable outcome was associated with cerebral perfusion pressure more than 40 mmHg in the operating room and intensive care unit, and not having surgery.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Evidence suggests that prehospital intubation is associated with poor outcomes in people with traumatic brain injury. Although some studies noted adjustment for confounding factors in their abstracts, it is difficult to determine whether there is an adverse effect of intubation, or whether intubation is an indicator of more severe injury.

One study found that avoiding prehospital hypoxia was associated with improved survival, which supports the need to manage airways effectively. The current recommendation to 'treat first the greatest threat to life' therefore

remains appropriate, and this may involve intubation. NICE guidance on assessment and initial management of major trauma (NG39) has further recommendations in this area.

New evidence is unlikely to change guideline recommendations.

### *Paramedic or physician emergency care*

**Surveillance summary (2017)**

An RCT[13] (HIRT) assessed standard paramedic treatment compared with standard treatment plus a physician arriving by helicopter in people with blunt trauma severe brain injury. This was originally defined as a GCS less than 9 but this was modified to also include people with GCS less than 13 plus an Abbreviated Injury Scale (AIS) score for the head region of more than 3. Intention-to-treat and as-treated analyses were pre-planned to deal with non-compliance with allocated treatment. The original definition of severe head injury was met by 375 patients, of whom 197 received physician treatment. Intention to treat analysis showed no significant effect of physician treatment on 6-month Glasgow Outcome Scale scores, or 30-day mortality. As-treated analysis showed significantly reduced 30-day mortality with physician treatment. The modified definition of head injury applied to 338 patients, of whom 182 were allocated to physician care. Neither the intention to treat nor the as-treated analyses of this group showed a significant effect of physician treatment compared with paramedic care.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Evidence on the impact of physicians as emergency response seems to be inconsistent, with no effect seen of most of the outcomes assessed. However, the change in definition of severe head injury and non-compliance with allocated treatment mean that the results from this study may not be robust.

New evidence is unlikely to change guideline recommendations.

## 176 – 03 What is the effectiveness of pre-hospital assessment tools for selecting adults, infants and children with head injury, for transport direct to specialist neuroscience care or a major trauma centre with neuroscience if the nearest hospital does not provide these?

### Recommendations derived from this review question

**Transport to hospital**

1.2.14 Transport patients who have sustained a head injury directly to a hospital that has the resources to further resuscitate them and to investigate and initially manage multiple injuries. All acute hospitals receiving patients with head injury directly from an incident should have these resources, which should be appropriate for a patient's age.** [new 2014]

** In the NHS in England these hospitals would be trauma units or major trauma centres. In the NHS in Wales this should be a hospital with equivalent capabilities.

**Training for ambulance crews**

1.2.15 Ambulance crews should be fully trained in the use of the adult and paediatric versions of the GCS and its derived score. [2003]

1.2.16 Ambulance crews should be trained in the safeguarding of children and vulnerable adults and should document and verbally inform emergency department staff of any safeguarding concerns. [2003, amended 2014]

## Surveillance decision

This review question should not be updated.

### *Transfer to neuroscience centres*

**Surveillance summary (2017)**

A systematic review and meta-analysis[14] assessed the evidence for direct transport to specialist centres compared with initial stabilisation at non-specialist centres for major trauma or moderate-to-severe head injury. Of 11 studies of head injury, all excluded patients not transferred to specialist centres and half were in remote locations. There was no significant difference in mortality between location of initial triage in adjusted or unadjusted analyses.

A cluster RCT[15] (HITS-NS) of 74 ambulance stations assessed standard admission to nearest non-specialist acute hospital compared with direct transfer to neuroscience centres in people with signs of isolated traumatic brain injury, and who had stable airway, breathing and circulation. Overall, 56 clusters recruited 293 patients in 12 months (169 intervention, 124 control) and overall compliance was 62%, but was 90% in the control arm. Non-compliance appeared to be driven by the perception of greater distance to neuroscience centres and of greater injury severity. CT showed traumatic brain injury in less than 25% of patients, 7% of whom needed neurosurgery. No significant differences in 30-day mortality were seen between the interventions.

A cohort study[16] included 7,149 people with traumatic brain injury who were transported directly to neuroscience centres (instead of the nearest hospital with emergency services). The emergency medical services time interval for transport was not significantly associated with mortality.

**Topic expert feedback**

Topic experts highlighted the cluster RCT[15] on transfer to specialist neuroscience centres or non-specialist centres.

**Impact statement**

Current evidence suggests no benefit to patients of initial admission to a neuroscience centre when traumatic brain injury is suspected. Therefore, current recommendations to transport patients to a hospital with facilities to resuscitate and manage multiple injures remains appropriate.

However, RCTs in this area have encountered practical difficulties, so they also cannot be considered to show definitive results.

The need to update recommendations in this area has lessened because trauma services have been undergoing changes such that people with life-threatening trauma would now primarily be transferred to a major trauma centre. The full version of the NICE guideline on major trauma defines major trauma centres as providing 'all the major specialist services relevant to the care of major trauma, that is, general, emergency medicine, vascular, orthopaedic, plastic, spinal, maxillofacial, cardiothoracic and neurological surgery and interventional radiology, along with appropriate supporting services, such as critical care'.

New evidence is unlikely to change guideline recommendations.

### *Identifying patients needing neurosurgical intervention*

**Surveillance summary (2017)**

A diagnostic study[17] included 3,628 people with suspected traumatic brain injury and assessed the HITS-NS triage rule compared with a reference standard of significant traumatic brain injury, defined an AIS score of at least 3 or neurosurgical intervention. Data from the HITS-NS trial, the Trauma Audit and Research Network registry and the North East Ambulance service database were included. The HITS-NS triage tool had sensitivity of 28.3% and specificity of 94.4.

A diagnostic cohort study[18] included 6,559 people with suspected head injury. The performance of the London Ambulance Service (LAS) and Head Injury Transportation Straight to Neurosurgery study (HITS-NS) triage criteria were assessed against a reference standard of traumatic brain injury defined as AIS for the

head region of greater than 3 or neurosurgical intervention. LAS had sensitivity of 44.5% and HITS-NS had sensitivity of 32.6%. False-negative cases were more likely to be women, and to have had low-level falls, and were less likely to have AIS head region scores of 5 or 6.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Currently, no recommendations cover methods of identifying people who need neurosurgery and thus may benefit from direct transport to a neuroscience centre. However, the low sensitivity of clinical decision rules for detecting patients who would benefit from transport to neurosurgical centres suggests that a considerable proportion of people with significant traumatic brain injury would not be triaged directly to a neuroscience centre.

New evidence is unlikely to change guideline recommendations.

## *Assessment in the emergency department*

### 176 – 04 Good practice in emergency department assessment

#### Recommendations derived from this review question

1.3.1 Be aware that the priority for all emergency department patients is the stabilisation of airway, breathing and circulation (ABC) before attention to other injuries. [2003]

1.3.2 Ascribe depressed conscious level to intoxication only after a significant brain injury has been excluded. [2003]

1.3.3 All emergency department clinicians involved in the assessment of patients with a head injury should be capable of assessing the presence or absence of the risk factors for CT head and cervical spine imaging listed in recommendations 1.4.7–1.4.12 and recommendations 1.5.8–1.5.14. Training should be made available as required to ensure that this is the case. [2003]

1.3.4 Patients presenting to the emergency department with impaired consciousness (GCS less than 15) should be assessed immediately by a trained member of staff. [2003]

1.3.5 In patients with GCS 8 or less, ensure there is early involvement of an anaesthetist or critical care physician to provide appropriate airway management, as described in recommendations 1.7.7 and 1.7.8, and to assist with resuscitation. [2003]

1.3.6 A trained member of staff should assess all patients presenting to an emergency department with a head injury within a maximum of 15 minutes of arrival at hospital. Part of this assessment should establish whether they are high risk or low risk for clinically important brain injury and/or cervical spine injury, using recommendations 1.4.7–1.4.12 and recommendations 1.5.8–1.5.14. [2003]

1.3.7 In patients considered to be at high risk for clinically important brain injury and/or cervical spine injury, extend assessment to full clinical examination to establish the need to request CT imaging of the head and/or imaging of the cervical spine and other body areas. Use recommendations 1.4.7–1.4.12 and recommendations 1.5.8–1.5.14 as the basis for the final decision on imaging after discussion with the radiology department. [2003, amended 2007]

1.3.8 Patients who, on initial assessment, are considered to be at low risk for clinically important brain injury and/or cervical spine injury should be re-examined within a further hour by an emergency department clinician. Part of this assessment should fully establish the need to request CT imaging of the head and/or imaging of the cervical spine. Use recommendations 1.4.7–1.4.12 and recommendations 1.5.8–1.5.14 as the basis for the final decision on imaging after discussion with the radiology department. [2003, amended 2007]

1.3.10 Manage pain effectively because it can lead to a rise in intracranial pressure. Provide reassurance, splintage of limb fractures and catheterisation of a full bladder, where needed.

Treat significant pain with small doses of intravenous opioids titrated against clinical response and baseline cardiorespiratory measurements.† [2007]

1.3.12 Throughout the hospital episode, use a standard head injury proforma in documentation when assessing and observing patients with head injury. This form should be of a consistent format across all clinical departments and hospitals in which a patient might be treated. Use a separate proforma for those under 16 years. Areas to allow extra documentation should be included (for example, in cases of non-accidental injury). Examples of proforma that should be used in patients with head injury are provided in appendix O of the full guideline. [2003, amended 2007]

† At the time of publication (January 2014), intravenous opioids did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## 176 – 05 Re-attendees

### Recommendations derived from this review question

1.3.9 Patients who return to an emergency department within 48 hours of transfer to the community with any persistent complaint relating to the initial head injury should be seen by or discussed with a senior clinician experienced in head injuries, and considered for a CT scan. [2003]

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## 176 – 06 Safeguarding and initial investigations

### Recommendations derived from this review question

1.3.11 A clinician with training in safeguarding should be involved in the initial assessment of any patient with a head injury presenting to the emergency department. If there are any concerns identified, document these and follow local safeguarding procedures appropriate to the patient's age. [2003, amended 2014]

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## 176 – 07 Involving neurosurgical care

### Recommendations derived from this review question

1.3.13 Discuss with a neurosurgeon the care of all patients with new, surgically significant abnormalities on imaging. The definition of 'surgically significant' should be developed by local neurosurgical centres and agreed with referring hospitals, along with referral procedures. [2003, amended 2014]

1.3.14 Regardless of imaging, other reasons for discussing a patient's care plan with a neurosurgeon include:

- Persisting coma (GCS 8 or less) after initial resuscitation.
- Unexplained confusion which persists for more than 4 hours.
- Deterioration in GCS score after admission (greater attention should be paid to motor response deterioration).
- Progressive focal neurological signs.
- A seizure without full recovery.
- Definite or suspected penetrating injury.
- A cerebrospinal fluid leak. [2003]

### Surveillance decision

This review question should not be updated.

---

#### *Early or late neurosurgery*

**Surveillance summary (2017)**

An RCT[19] (STITCH; n=170) assessed early surgery (within 12 hours) compared with initial conservative treatment in people with intracerebral haematoma that did not need urgent surgery. The primary outcome was the proportion of patients with favourable recovery. The study intended to enrol 840 participants, but was stopped early because of low recruitment. A greater proportion of people in the early surgery group had a favourable outcome, but this was not significant, which the authors noted was probably due to the lower than planned sample size. Mortality was significantly higher in the conservative treatment group. However, the authors noted that further research was needed. A further publication of this study, which reported the same results[20] was also identified.

A systematic review and meta-analysis[21] of 5 studies assessed early decompressive craniectomy (within 12 hours of injury) compared with late surgery in people with traumatic brain injury. Early surgery was not associated with significant effects on mortality or outcome. Bilateral pupil abnormality was significantly associated with increased mortality and unfavourable outcome.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

In developing the 2007 version of the guideline, a research recommendation was made requesting research 'to develop consensus on criteria for lesions not currently considered to be surgically significant following imaging of a patient with head injury'.

This research recommendation was made after research showed benefits of early surgical evacuation of spontaneous intracerebral haemorrhages. The STITCH trial therefore assessed this intervention in a trauma population.

The guideline noted that early neurosurgery would 'fundamentally alter the recommendations made by NICE, in terms of which patients are referred to neurosurgery, and more importantly, how they should be managed there'.

However, results of the STITCH trial were not available for consideration during development of NICE CG176. The results suggest that there may be a significant mortality benefit of early neurosurgery; however, the effect on outcome did not reach statistical significance. The study was limited by low recruitment, which led to early closure of the trial, and thus the required sample size was not met. It is unlikely that new recommendations in this area could be made with the current evidence.

New evidence is unlikely to change guideline recommendations.

---

### *Neurosurgical consultation in minor traumatic brain injury*

**Surveillance summary (2017)**

A retrospective analysis[22] included 270 people with mild traumatic brain injury and minor intracranial injury on CT. Of this sample, 90 had a neurosurgical consultation and 180 were managed without neurosurgical consultation. No patients in either group had neurosurgical intervention, in-hospital mortality or readmission within 30 days. There was no significant difference between the groups in the number of people who returned to the emergency department after discharge.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

The evidence suggests that neurosurgical consultation is not beneficial for patients with minor traumatic brain injury. However, this evidence would not affect the recommendation to seek neurosurgical advice in the presence of surgically significant imaging findings or signs of more serious injury.

New evidence is unlikely to change guideline recommendations.

---

## *Investigating clinically important brain injuries*

**176 – 08 What is the best initial diagnostic technique to determine which patients have sustained damage to the head and require further assessment of the head?**

### Recommendations derived from this review question

1.4.1 The current primary investigation of choice for the detection of acute clinically important brain injuries is CT imaging of the head. [2003]

1.4.2 For safety, logistic and resource reasons, do not perform magnetic resonance imaging (MRI) scanning as the primary investigation for clinically important brain injury in patients who have sustained a head injury, although it is recognised that additional information of importance to the patient's prognosis can sometimes be detected using MRI. [2003]

1.4.3 Ensure that there is appropriate equipment for maintaining and monitoring the patient within the MRI environment and that all staff involved are aware of the dangers and necessary precautions for working near an MRI scanner. [2003]

1.4.4 Do not use plain X-rays of the skull to diagnose significant brain injury without prior discussion with a neuroscience unit. However, they are useful as part of the skeletal survey in children presenting with suspected non-accidental injury. [2007]

1.4.5 If CT imaging is unavailable because of equipment failure, patients with GCS 15 may be admitted for observation. Arrangements should be in place for urgent transfer to a centre with CT scanning available should there be a clinical deterioration that indicates immediate CT scanning is necessary. [2007]

## Surveillance decision

This review question should not be updated.

### *Choice of imaging*

**Surveillance summary (2017)**

A retrospective cross-sectional study[23] included 177 children with suspected intentional head trauma who had skull X-ray and CT with 3D reconstruction. X-ray showed skull fracture in 67% of children. CT with 3D reconstruction had sensitivity of 97% and specificity of 94%. There was no significant difference between X-ray and 3D CT results.

A retrospective study[24] included 221 children younger than 3 years with head trauma. Unenhanced axial CT was reviewed then images with additional multiplanar reconstruction were reviewed. Multiplanar reconstruction detected haemorrhage in an additional 6.5% of children, detected additional incidental findings in 2.3% of children, and helped to confirm presence of artefacts in 2.3% of children.

A cohort study[25] included 69 children and young people (aged under 21 years) with suspected head injury who were assessed with CT and point-of-care ultrasound. Emergency physicians had a 1-hour training session before using the ultrasound. Skull fracture was present in 8% of the sample. Ultrasound had sensitivity of 88%, specificity of 97%, positive likelihood ratio of 27 and negative likelihood ratio of 0.13.

A retrospective study[26] included 103 children with minor head injury who had initial CT and follow-up rapid MRI within 48 hours. Imaging was reviewed by a blinded neuroradiologist. Agreement between CT and rapid MRI was high for extra-axial haemorrhage (kappa=0.84), substantial for haemorrhagic contusion or intraparenchymal haemorrhage (kappa=0.61) and for skull fracture (kappa=0.71), but poor for diffuse axonal injury (kappa = 0.154).

A retrospective study[27] included 315 people with trauma who underwent CT of the brain and also had spiral facial CT. Spiral facial CT had sensitivity of 92.2%, specificity of 98.1%, positive predictive value of 95.9%, and negative predictive value of 96.3%, using standard CT as the reference standard.

A cohort study[28] included 394 people with closed head injury who had CT and brain electrical activity recorded from electrodes on the forehead. Overall, 29% had positive findings on CT, and 12% had traumatic intracranial haematoma. People with negative CT findings were used as the control group. A previously developed algorithm (TBI-Index) was used to estimate CT findings from forehead electrical activity. TBI-Index had sensitivity 95.7% of and specificity of 43.9% for detecting haematoma. The TBI-Index was not significantly affected by distance of the bleed from the recording site or by the volume of blood.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Several studies assessing the effectiveness of imaging methods compared with CT were identified. However, all studies included small sample sizes, and no method of imaging was covered by more than 1 study, or reported on additional outcomes of interest in developing the guideline (for example, mortality, disability, neurological outcome, hospital duration, and cost). This evidence base is likely to be insufficient for formulating recommendations at this time.

The study showing that 3D CT effectively identified skull fracture in children lends some support to the recommendation not to use plain X-rays for diagnosis of brain injury.

New evidence is unlikely to change guideline recommendations.

## 176 – 09 What is the best clinical decision rule for selecting adults, infants and children with head injury for CT head scan?

### Recommendations derived from this review question

1.4.7 For adults who have sustained a head injury and have any of the following risk factors, perform a CT head scan within 1 hour of the risk factor being identified:

- GCS less than 13 on initial assessment in the emergency department.
- GCS less than 15 at 2 hours after the injury on assessment in the emergency department.
- Suspected open or depressed skull fracture.
- Any sign of basal skull fracture (haemotympanum, 'panda' eyes, cerebrospinal fluid leakage from the ear or nose, Battle's sign).
- Post-traumatic seizure.
- Focal neurological deficit.
- More than 1 episode of vomiting.

A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

1.4.8 For adults with any of the following risk factors who have experienced some loss of consciousness or amnesia since the injury, perform a CT head scan within 8 hours of the head injury:

- Age 65 years or older.
- Any history of bleeding or clotting disorders.
- Dangerous mechanism of injury (a pedestrian or cyclist struck by a motor vehicle, an occupant ejected from a motor vehicle or a fall from a height of greater than 1 metre or 5 stairs).
- More than 30 minutes' retrograde amnesia of events immediately before the head injury.

A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

1.4.9 For children who have sustained a head injury and have any of the following risk factors, perform a CT head scan within 1 hour of the risk factor being identified:

- Suspicion of non-accidental injury
- Post-traumatic seizure but no history of epilepsy.
- On initial emergency department assessment, GCS less than 14, or for children under 1 year GCS (paediatric) less than 15.
- At 2 hours after the injury, GCS less than 15.
- Suspected open or depressed skull fracture or tense fontanelle.
- Any sign of basal skull fracture (haemotympanum, 'panda' eyes, cerebrospinal fluid leakage from the ear or nose, Battle's sign).
- Focal neurological deficit.
- For children under 1 year, presence of bruise, swelling or laceration of more than 5 cm on the head.

A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

1.4.10 For children who have sustained a head injury and have more than 1 of the following risk factors (and none of those in recommendation 1.4.9), perform a CT head scan within 1 hour of the risk factors being identified:

- Loss of consciousness lasting more than 5 minutes (witnessed).
- Abnormal drowsiness.
- Three or more discrete episodes of vomiting.
- Dangerous mechanism of injury (high-speed road traffic accident either as pedestrian, cyclist or vehicle occupant, fall from a height of greater than 3 metres, high-speed injury from a projectile or other object).
- Amnesia (antegrade or retrograde) lasting more than 5 minutes.*

  A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

* Assessment of amnesia will not be possible in preverbal children and is unlikely to be possible in children aged under 5 years.

1.4.11 Children who have sustained a head injury and have only 1 of the risk factors in recommendation 1.4.10 (and none of those in recommendation 1.4.9) should be observed for a minimum of 4 hours after the head injury. If during observation any of the risk factors below are identified, perform a CT head scan within 1 hour:

- GCS less than 15.
- Further vomiting.
- A further episode of abnormal drowsiness.

  A provisional written radiology report should be made available within 1 hour of the scan being performed. If none of these risk factors occur during observation, use clinical judgement to determine whether a longer period of observation is needed. [new 2014]

## Surveillance decision

This review question should not be updated.

---

### *Decision rules for adults*

**Surveillance summary (2017)**

A diagnostic study[29] assessed the ability of handheld quantitative electroencephalogram (EEG) to predict intracranial lesions in 152 adults presenting with acute mild traumatic brain injury. Of the sample, 17.1% had positive CT findings. Handheld quantitative EEG was compared with New Orleans Criteria (NOC), Canadian CT Head Rule (CCHR), and National Emergency X-Radiography Utilization Study II (NEXUS II) Rule. A 10-minute handheld quantitative EEG reading was taken for each patient and a discriminant score cut-off of 31 was chosen, with an AUC of 0.84.

- Handheld quantitative EEG had sensitivity of 92.3% and specificity of 57.1%.
- NOC had sensitivity of 96.1% and specificity of 15.8%.
- CCHR had sensitivity of 46.1% and specificity of 86.5%.
- NEXUS II had sensitivity of 96.1% and specificity of 31.7%.

A retrospective cohort study[30] included 474 people with minor head injury to evaluate the CCHR and the NOC in predicting clinically important brain injury on CT and need for neurosurgery. Of the cohort, 16.2% had clinically important brain injury and 2.3% needed neurosurgery.

For clinically important brain injury:

- The CCHR had sensitivity of 80%, specificity of 39%, and negative predictive value of 88%.
- The NOC had sensitivity of 92%, specificity of 17%, and negative predictive value of 91%.

For neurosurgery:

- The CCHR had sensitivity of 80%, specificity of 36%, and negative predictive value of 99%.

- The NOC had sensitivity of 100%, specificity of 15%, and negative predictive value of 100%.

Of missed cases, 88% assessed by CCHR and 83% assessed by NOC reported loss of consciousness.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Studies of clinical decision rules showed results that broadly align with the data assessed when developing the guideline. Most decision rules have high sensitivity with moderate specificity and increasing specificity generally results in lower sensitivity. The guideline considered sensitivity to be the most important outcome because of the potentially severe consequences of not detecting clinically important brain injury.

Recommendations in NICE CG176 were based on the CCHR. Overall, current recommendations appear to adequately identify people who should have CT to determine whether they have clinically significant brain injury.

New evidence is unlikely to change guideline recommendations.

---

### *Decision rules for children*

**Surveillance summary (2017)**

An analysis of data from a prospective cohort study[31] included 42,041 children, of whom 10,499 were younger than 2 years, to assess the GCS and paediatric GCS for identifying traumatic brain injury. Standard GCS scores were obtained in those aged 2 years or older and the paediatric GCS was used in children younger than 2 years. In children older than 2 years, 6.5% had traumatic brain injury on CT, as did 9.4% of those aged younger than 2 years. In children older than 2 years, 1.8% had clinically important traumatic brain injury, as did 1.4% of those aged younger than 2 years. The paediatric GCS had an AUC of 0.61 for detecting traumatic brain injury and 0.77 for clinically important brain injury. The standard GCS had an AUC of 0.71 for detecting traumatic brain injury and 0.81 for clinically important brain injury.

A subgroup analysis of a cohort study[32] included 3,771 children with minor head trauma. Physicians were asked to predict the probability of brain injury visible on CT and brain injury needing intervention. The mean predicted risk of brain injury on CT was 4.6%, with an actual rate of 4.1%. The mean predicted risk of brain injury needing intervention was 1.4%, with an actual rate of 0.6%. However, in infants (age not defined in the abstract), physicians underestimated the need for intervention at 6.2%, with an actual rate of 12.3%.

An analysis of clinical decision rules[33] included 1,009 children (younger than 18 years) with minor head injury, of whom 2% had clinically important traumatic brain injury. The clinical decision rules assessed were the Canadian Assessment of Tomography for Childhood Head Injury (CATCH), Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE), and Pediatric Emergency Care Applied Research Network (PECARN). Additionally assessed were 2 measures of physician judgment: an estimate of less than 1% risk of traumatic brain injury and CT ordering practice.

- PECARN had sensitivity of 100% and specificity of 62%.
- CATCH had sensitivity of 91% and specificity of 44%.
- CHALICE had sensitivity of 84% and specificity of 85%.
- Physicians' estimate had sensitivity of 95% and specificity of 68%.
- Physicians' CT ordering practice had sensitivity 100% of and specificity of 50%.

A prospective cohort study[34] included children aged younger than 2 years with head trauma and aimed to derive and validate a model to identify skull fracture. Children at high risk of clinically important traumatic brain injury were excluded. The rule had sensitivity 94% of and specificity of 86% in the derivation phase (n=811) and had sensitivity of 89% and specificity of 87% in the validation phase (n=856). The authors noted that use of the rule

would have reduced radiological evaluations by about 60%.

A retrospective analysis[35] of 3,102 children with mild head trauma included a sample of 806 children aged 2 to 15 years. Children were assigned to a high or low risk category based on signs or symptoms. In the high risk group, 29.8% of CT findings showed pathology, whereas in the low risk group, 1.9% of CT findings showed pathology. Signs of traumatic brain injury included vomiting, suspected skull fracture, and loss of consciousness.

An analysis[36] included 42,112 children with minor blunt head trauma, 5,392 of whom had a history of vomiting with complete data, and 815 of this group had isolated vomiting. Brain injury was detected on CT in 1.7% of those with isolated vomiting and 6.4% of those whose vomiting was not the only sign of brain injury. Clinically important brain injury was detected in 0.2% of children with isolated vomiting and 2.5% of those whose vomiting was not the only sign of brain injury.

A cohort study[37] (n=12,675) included children (aged 2–18 years) with headaches after minor blunt head trauma and GCS of 14 or 15. Traumatic brain injury was seen on CT in 0.7% of children who had isolated headache, and 4.5% of children with non-isolated headache. No association between location or severity of headaches and CT findings was found.

A prospective cohort study[38] included 40,693 children with blunt head trauma and GCS of 14 or 15. Loss of consciousness occurred in 6,286 children; 0.5% of children with isolated loss of consciousness had clinically important brain injury. Isolated loss of consciousness was associated with significantly lower risk of clinically important brain injury than loss of consciousness plus other PECARN predictors. Clinically important brain injury was detected in 2.5% of children who had loss of consciousness and 0.5% of children with no history of losing consciousness.

A secondary analysis of a prospective cohort study[39] included 43,399 children aged younger than 18 years with minor blunt head trauma; 1,297 children had a guardian report of the child behaving abnormally. Abnormal behaviour was the only sign of traumatic brain injury in 31.7% of such patients, and only 0.2% of this group had clinically important traumatic brain injury. In children with abnormal behaviour plus other signs of brain injury, clinically important brain injury was identified in 3.3%. A larger proportion of children had brain injury detected that was not deemed to be clinically important: 2.2% of children with isolated abnormal behaviour and 9.8% of those with abnormal behaviour plus other signs of brain injury.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Several studies evaluating clinical decision-making in children were identified and broadly agree with the guideline in several respects:

- GCS and physicians' estimate of risk of brain injury appear to be insufficient.
- Available clinical decision rules generally have high sensitivity with moderate specificity.
- Children with an isolated sign or symptom of brain injury have a very low risk of clinically significant brain injury.

These findings generally support the current recommendations, which were based on the CHALICE rule. However, one study found this rule to have lower sensitivity than other available rules. This is potentially concerning, but the population of around 1,000 children in the study is very small compared with the population (over 22,000) in the main study of CHALICE considered when developing the guideline.

New evidence is unlikely to change guideline recommendations.

---

### *Computerised decision support*

**Surveillance summary (2017)**

A cohort study[40] assessed the effect of computerised decision support on CT orders for mild traumatic brain injury. The number of people included was not reported in the abstract. After implementation of the computerised decision support system, the proportion of CT scans ordered for people with suspected mild traumatic brain injury fell significantly from 58.1% to 50.3%. There was

no significant change in the control group, but the abstract did not provide a description of the control group. CT in the subsequent 7 days was not significantly increased after implementing the computerised decision support tool.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

The guideline has no recommendations on use of computerised decision support tools.

Evidence suggests that computerised decision support tools may result in reductions in CT. However, the lack of clarity about the control group, lack of relevant diagnostic outcomes or description of how the tool worked limits the impact of the results on the guideline.

New evidence is unlikely to change guideline recommendations.

---

### *Interpretation of imaging*

**Surveillance summary (2017)**

A prospective study[41] included people with compound head injury, and aimed to validate a new grading system for such injuries. Of the sample assessed:

- 53% had grade 1 injury, no dural violation or midline shift
- 16% had grade 2 injury, cerebrospinal fluid leak or pneumocephalus
- 10% had grade 3 injury with exposed brain
- 14% had grade 4 injury with exposed brain
- 7% had grade 5 injury, exposed brain and midline shift.

In multivariate analysis, increasing grade of injury was associated with significant increases in infectious complications, unfavourable outcome, delayed seizures, and length of stay in hospital.

A cohort study[42] included 156 children aged younger than 2 years with mild head trauma who underwent CT. Emergency physicians interpreted the results and the findings were compared with radiologists' interpretation of the same scans. The emergency physicians' interpretations had an AUC of 0.86, sensitivity of 76.9% and specificity of 95.1%.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Evidence suggests that a system of grading compound head injuries correlates with outcomes. It is unlikely that the guideline would need to be updated to incorporate this grading system because all people with compound (that is, open) head injuries should receive CT.

A study assessing the accuracy of emergency department physicians' interpretation of CT findings suggests that emergency department physicians may miss some CT findings. However these findings may not be generalisable beyond the study population of children aged under 2 years. This provides some support for the recommendations to provide provisional written radiology reports within 1 hour of CT.

New evidence is unlikely to change guideline recommendations.

---

**176 – 10 What is the best clinical decision rule for selecting adults, infants and children with head injury for CT head scan who have no history of amnesia or loss of consciousness who are on anticoagulant or antiplatelet therapy?**

## Recommendations derived from this review question

Recommendations 1.4.7–1.4.11 (see above) also apply to this review question. An additional recommendation was made.

1.4.12 For patients (adults and children) who have sustained a head injury with no other indications for a CT head scan and who are having warfarin treatment, perform a CT head scan within 8 hours of the injury. A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

## Surveillance decision

This review question should not be updated.

An editorial correction is needed to include a cross-reference in recommendation 1.4.12 to the more recent guideline on blood transfusion (NICE NG24), which has recommendations on reversal of warfarin anticoagulation in people with suspected traumatic intracranial haemorrhage.

---

### *Antiplatelet and anticoagulant drugs*

**Surveillance summary (2017)**

*Anticoagulants*

The UK-based AHEAD study[43] included 3,566 people with blunt head injury who were taking warfarin at the time of injury. CT was performed in 59.8% of participants and showed significant head injury-related finding in 5.4%; 0.5% underwent neurosurgery; 1.2% patients suffered a head injury-related death. Overall, the rate of adverse outcome was 5.9%. Patients with GCS of 15 and no associated symptoms had lowest risk of adverse outcome (2.7%). Multivariable analysis found risk of adverse outcome to increase when reporting at least one associated symptom (vomiting, amnesia, headache, or loss of consciousness). INR measurement did not predict adverse outcome in patients with GCS of 15. A cost-effectiveness analysis based on the data from AHEAD[44] suggested that CT in all people on warfarin presenting with head injury was not cost-effective, with and an incremental cost-effectiveness ratio (ICER) of £94,895.

A retrospective study[45] (n=70) included people with mild traumatic brain injury and traumatic intracranial haemorrhage. Before head injury, 37 had no antithrombotic use, 22 people used antiplatelet agents, and 6 people were on rivaroxaban. Despite the small number of people on rivaroxaban, its use was associated with higher mortality and recurrent haemorrhage. However, no differences in length of hospital stay or GCS at discharge were seen.

A systematic review and meta-analysis[46] assessed 7 studies (n=1,594) of a second CT after 24 hours in people taking vitamin K antagonists at the time of head trauma whose initial scan was normal. The incidence of haemorrhage on the second scan was 0.6%.

A retrospective analysis[47] included 303 people with blunt head trauma, 168 of whom were taking antiplatelet or anticoagulant drugs. Aspirin was used by 72 people, clopidogrel by 39 people, and warfarin by 18 people. Initial CT showed 'significant findings' in 166 people (98.8%). Delayed intracranial haemorrhage was seen on second CT in 2 people, both of whom were taking warfarin (1.2%) and had INR greater than 2.0.

An analysis[48] included 42 people who had traumatic brain injury, were taking warfarin at the time of injury, had INR of 1.5 or higher, and received at least 1 dose of three-factor prothrombin complex concentrate. A moderate dose of prothrombin complex concentrate (35 IU/kg) was used in 17 people, and 25 people received a low dose (25 IU/kg). The low dose was associated with significantly lower

rates of INR reversal at first measurement after administration of prothrombin complex concentrate. The low dose was also associated with significantly longer time to reversal of INR. There were no differences between the groups in stabilisation of brain injury, days in the intensive care unit, total days in hospital, blood product administration, and adverse events.

A retrospective analysis[49] assessed 298 people who had minor head injury with normal CT findings who were on warfarin. Of this group, (3.7%) had a second CT, with 1 (0.3%) abnormality. Fresh frozen plasma was administered to 7 people (2.4%), and 8 (2.7%) received vitamin K. One patient (0.3%) needed neurosurgical intervention. The median hospital length of stay was 3 days. No patients re-attended 2 weeks after discharge.

A retrospective cohort study[50] included 10,782 people aged 65 years or older admitted to hospital with traumatic brain injury who were on warfarin in the month before their injury. The study looked at the effects of warfarin use in 30-day periods in the year after brain injury. Warfarin use 'in the prior period' was associated with decreased risk of thrombotic events, and of haemorrhagic or ischemic stroke, but with increased risk of haemorrhagic events.

*Antiplatelet agents*

A systematic review and meta-analysis[51] assessed 10 studies (n=20,247) investigating the effect of pre-injury antiplatelet therapy in people with traumatic head injury. Antiplatelet therapy was associated with significantly increased risk of traumatic intracranial haemorrhage. The risk was highest for mild traumatic brain injury. Although there was substantial heterogeneity between the studies, the authors noted that most individual results showed the association between antiplatelets and intracranial haemorrhage. However, aspirin monotherapy showed no significant effect on risk of intracranial haemorrhage.

A systematic review[52] assessed 7 retrospective cohort studies of platelet transfusion in people with antiplatelet-agent-associated intracranial haemorrhage. Platelet transfusion was associated with significantly greater mortality, and greater likelihood of 'medical decline' in traumatic antiplatelet-agent-associated intracranial haemorrhage.

A prospective analysis[53] included 142 people with CT-confirmed traumatic intracranial haemorrhage, 71 of whom were on clopidogrel at the time of head injury. A matched sample of 71 people were not on clopidogrel. More than half of patients (61%) received a platelet transfusion. Pre-injury clopidogrel was associated with significantly greater likelihood of intracranial haemorrhage progression on repeat CT, needing repeat CT because of clinical deterioration, and neurosurgical intervention.

A prospective analysis[54] included 144 people with CT-confirmed traumatic intracranial haemorrhage, 72 of whom were on aspirin at the time of head injury. A matched sample of 72 people were not on aspirin. There were no significant differences between groups for progression on repeat CT, or change in management after repeat CT. CGS at discharge and mortality also did not differ significantly between groups.

A prospective analysis[55] included 264 people with CT-confirmed intracranial haemorrhage who were taking aspirin or clopidogrel, or both at the time of head injury. Platelet counts of 135,000 per microliter of blood of less were associated with significantly greater likelihood of progression of intracranial haemorrhage on repeat CT. Platelet counts of 95,000 per microliter of blood of less were associated with significantly greater likelihood of need for neurosurgical intervention.

*Anticoagulants and antiplatelets*

A retrospective analysis[56] included 198 people older than 60 years with external signs of head trauma. Antithrombotic drugs (defined as warfarin, clopidogrel and aspirin) were used at the time of head injury in 64% of the cohort. The rate of intracranial haemorrhage did not differ significantly with antithrombotic use compared with no antithrombotic use. No differences were seen in neurological complications defined as progression of intracranial haemorrhage, craniotomy, neurological deterioration, or death.

A retrospective analysis[57] included 1,552 people older than 65 years with closed head injury and evidence of brain haemorrhage on CT. Antithrombotic agent use was: 543 on aspirin only, 97 on clopidogrel only, 218 on warfarin only, 193 on clopidogrel and aspirin, and 501 on no antithrombotic agent. Blood products were administered to reverse coagulopathy in 77.3% of people on antithrombotic medications. Antithrombotics were associated with increased mortality.

Warfarin was associated with a borderline significant increase in mortality compared with other oral anticoagulants.

A retrospective analysis[58] included 1,606 people with blunt head injury, 508 of whom had CT-confirmed intracranial haemorrhage, and 72 people from this group were taking warfarin, aspirin, or clopidogrel at the time of injury. People on these drugs were significantly older, and presented with worse injury, and had longer stays in intensive care and in hospital. They were also significantly more likely to have progression of intracranial haemorrhage on repeat CT.

A retrospective analysis[59] assessed 144 people on anticoagulant and antiplatelet drugs who had head injury and a routine second non-contrast CT 6 hours after the first. Intracranial haemorrhage was detected in 10 people, and 1 person had delayed intracranial haemorrhage, but did not need further intervention.

A retrospective study[60] included 77 people with isolated head injury, 27 of whom who were taking clopidogrel or warfarin at the time of injury. People on preinjury clopidogrel or warfarin were significantly older than the control group and were significantly more likely to have an unfavourable outcome at 6 months.

*Ibuprofen*

An analysis[61] assessed the effect of preinjury ibuprofen use in 195 people with traumatic intracranial haemorrhage. People with preinjury ibuprofen use were matched to 2 non-ibuprofen control patients. There was no evidence of an effect of ibuprofen on haemorrhagic progression on repeat CT or need for neurosurgical intervention.

**Topic expert feedback**

Topic experts highlighted the AHEAD study,[43] which was noted as ongoing at the time of developing the guideline.

Topic expert feedback suggested that preinjury clopidogrel use may be associated with increased risk of poor outcomes after head injury.

**Impact statement**

*Anticoagulants*

Warfarin was noted to increase risk of intracranial haemorrhage after head injury, which is consistent with current recommendations to perform CT in people on warfarin in the absence of any signs of brain injury. Additionally, the AHEAD study indicated that the risk of adverse outcomes (neurosurgery or death. was greater when patients had at least 1 symptom). It identified that 2.7% of people on warfarin with no indications for CT had an adverse outcome. This provides some support for the recommendation to do CT in people on warfarin in the absence of other indications for CT. The proportion of people with significant head injuries but no symptoms was lower than the 5.5% found in the evidence considered in guideline development. However, none of the studies identified in surveillance assessed the risk of significant head injury in people without symptoms in people on warfarin compared with those not on warfarin.

*Antiplatelets*

A large systematic review suggested that antiplatelet drugs (other than aspirin) may increase the risk of intracranial haemorrhage after head injury. However, several of the studies included in this review were excluded from consideration during guideline development.

During surveillance, several studies were identified that reported on both warfarin and antiplatelets. It was not clear from the abstracts whether data for clopidogrel could be extracted separately from such studies.

In developing the guideline, the guideline committee considered evidence on clopidogrel, but excluded all identified evidence from the clinical review because it did not meet the protocol '(indirect population, included patients on warfarin or clopidogrel, not all patients were scanned or unknown if they had initial loss of consciousness or amnesia that is, whether they would have been scanned under 2007 NICE recommendations)'.

The studies identified in surveillance also would not have met the criteria for the protocol. They provide evidence that anticlotting drugs may be associated with higher risk of intracranial haemorrhage or poorer outcomes. But we do not know whether significant brain injuries would be missed in this group of patients with the current criteria for CT.

*Other considerations*

We considered whether the review protocol for this review question needed to change in light of the poor evidence available. However, the AHEAD study of warfarin showed that a small proportion of people on warfarin who would be

missed by the general CT criteria do have significant brain injury. This supports the recommendation to undertake CT in people on warfarin. Similar studies evaluating antiplatelets agents and also direct oral anticoagulants are needed. Although the evidence is insufficient to support an update at this time, we will reconsider this decision if suitable new evidence emerges.

The cost-effectiveness study showing CT in all people with head injury on warfarin was considered not to have an impact on current recommendations because:

- it was based on a very small number of people that may not fully represent the target population
- exploration of the uncertainty around the ICER was insufficient.

New evidence is unlikely to change guideline recommendations.

---

### *Coagulopathy*

**Surveillance summary (2017)**

A systematic review and meta-analysis[62] assessed 19 studies of traumatic brain injury and coagulopathy. Studies were included if they assessed coagulopathy by comparing isolated traumatic brain injury with a similar severity of injury to other body regions, or compared progressive haemorrhagic injury with non-progressive head injury. Mean fibrinogen was significantly higher in people with isolated traumatic brain injury, compared with traumatic brain injury plus other injuries or other injuries only. However, other coagulation tests were not significantly different between these groups. People with progressive haemorrhagic injury had a lower platelet count and a higher international normalised ratio in people whose injury did not progress, but no differences were seen in the mean activated partial thromboplastin time or prothrombin time.

An analysis[63] included 279 people with isolated traumatic brain injury; 157 of whom had progressive haemorrhagic injury and 122 of whom were stable on repeat CT. Patients with progressive head injury were older, had fewer hospital-free days, and higher mortality. Coagulopathy and age were independent predictors of progression. Controlling for age, CGS and coagulopathy, patients with intraparenchymal contusions were more likely to experience progressive haemorrhagic injury.

A retrospective analysis[64] including 342 people was used for validation of the IMPACT (International Mission for Prognosis and Analysis of Clinical Trials) clinical prediction model. The IMPACT model had an area under the curve (AUC) of 0.85 for predicting mortality, and 0.81 for predicting neurological outcome. People with poor outcomes had significantly lower levels of platelets and higher international normalised ratio (INR) and injury severity scores. These variables were added to the model. However, the only significant improvement in prediction was seen with adding INR to the model which improved prediction of mortality but not neurological outcome.

A prospective analysis[65] included 87 people with isolated traumatic brain injury and coagulopathy, of whom 49 were given blood products to reverse coagulopathy and 38 people also received low-dose (20 micrograms/kg) recombinant factor VIIa. People who received recombinant factor VIIa had significantly greater improvement in INR. Significantly more people who received only blood products developed progressive haemorrhagic injury compared with those receiving recombinant factor VIIa. There was no evidence of an effect on mortality with recombinant factor VIIa.

A retrospective cohort analysis[66] included 591 people with isolated traumatic brain injury who were not on pre-injury anticoagulant or antiplatelet therapy who had coagulation tests (INR, platelet count, and partial thromboplastin time) on admission. Coagulopathy was defined as an INR of 1.5 or greater, partial thromboplastin time of 35 seconds or greater, or platelet count of 100,000 per microlitre or less. Of the cohort, 13.3% showed coagulopathy at admission. A platelet count of 100,000 per microlitre or lower independently predicted progression on repeat CT, need for neurosurgical intervention, and mortality. INR independently predicted progression on repeat CT.

An analysis[67] included 81 people with isolated brain injury who underwent coagulation tests

on admission. Coagulopathy was defined as platelet count less than 120,000 per microlitre, INR greater than 1.2 or prolonged activated partial thromboplastin time greater than 40 seconds. People with coagulopathy had significantly lower factor VII activity than those with no coagulopathy. However, there was no evidence of a difference in mortality by factor VII activity.

A retrospective analysis[68] of data (n=647) from the COBRIT trial (Citicoline Brain Injury Treatment) assessed coagulopathy in people with isolated traumatic brain injury. Coagulopathy was defined as INR greater than 1.3, partial thromboplastin time greater than 38 seconds, or platelet count less than 120,000 per microlitre. Coagulation tests were performed at admission and during the first 7 days of hospital admission. Incidence of coagulopathy was highest at admission and on day 2. Of this cohort, 21% had coagulopathy, and these patients were significantly more likely to have GCS less than 8. This group also had higher mortality, poorer functional and cognitive outcomes, and had longer stay in hospital.

A retrospective analysis of a trauma registry[69] included 157 people with isolated traumatic brain injury and coagulopathy (defined as INR greater than 1.3). Procoagulant agents (fresh frozen plasma, platelets, cryoprecipitate, prothrombin complex concentrates, tranexamic acid, vitamin K) were used in 68 people. The median time to delivery of first procoagulant was 182.5 minutes, and time to normalisation of INR was 605 minutes. Normalisation of INR was independently associated with significantly lower mortality.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

NICE guidance on blood transfusion (NG24) contains recommendations for reversing anticoagulation for people on warfarin who have suspected traumatic intracranial haemorrhage. NICE NG24 also covers platelet transfusion

It was not always clear in the abstracts of the studies of coagulopathy whether patients were on anti-clotting drugs at the time of injury. One study looked specifically at people not taking such drugs, and suggested a fairly high incidence of coagulopathy of over 13%. It is also not clear whether coagulopathy occurred for the first time in head injury. People with a previous history of bleeding or clotting disorders would receive CT under current recommendations (see recommendation 1.4.8)

Detection and treatment of coagulopathy is not considered in NICE CG176, but may be relevant to acute care because of the long time between starting treatments to correct coagulopathy and seeing an effect. However, the available evidence consists of small observational studies, and do not show a clear need for updated guidance in this area.

New evidence is unlikely to change guideline recommendations.

---

**176 – 11 What is the diagnostic accuracy of biomarkers (S100B, NSE, GFAP) in the emergency department for selecting adults with head injury for CT head scan?**

## Recommendations derived from this review question

No recommendations were made for this review question. A research recommendation was made (see RR – 04 later in this document).

## Surveillance decision

This review question should not be updated.

---

**Surveillance summary (2017)**

*S100B*

A systematic review[70] of 22 studies evaluated S100B screening in people with mild traumatic brain injury who underwent CT. The number of participants in the included studies was not reported in the abstract. S100B concentration was significantly associated with positive findings on CT. There was a significant positive association between S100B protein concentration and positive CT scan (22 studies, SMD = 1.92, 95% CI = 1.29–2.45, $I^2$ = 100%; p < 0.001). A cut-point range of 0.16–0.20 micrograms/l had sensitivity of 98.65% and specificity of 50.69%, respectively. A threshold of S100B greater than 0.20 micrograms/l had sensitivity of 99.63% and specificity of 46.94%.

A prospective study[71] included 787 people with mild traumatic brain injury presenting within 6 hours of injury and 467 controls without head injury who had routine blood tests. Serum was analysed for S100B and apolipoprotein (apoA-I). Control blood values were used to define cut-offs.

- S100B had sensitivity of 25.2% and specificity of 89.9%
- AopA-I had sensitivity of 24.9% and specificity of 90.2%

The area under the curve for both tests combined was significantly higher than for either test alone.

The AUC for prediction of abnormal initial head CT scan using S100B was 69.4% and was not significant for apoA-I. At a cut-off of <0.060 micrograms/l, the sensitivity for abnormal head CT was 98%, and 22.9% of CT scans could have been avoided. There was significant variation in the accuracy of S100B with age and race.

A prospective study[72] included 251 people with suspected mild to moderate brain injury, of whom 14.3% had positive CT findings. Blood samples were obtained within 6 hours of injury and were tested for S100B, GFAP and UCHL-1. For discriminating between positive and negative CT findings:

- S100B had an AUC of 0.75. Sensitivity of 100% was seen at a cut-off of 30 pg/ml (0.03 micrograms/l), with specificity of 2%.
- GFAP had an AUC of 0.79. Sensitivity of 100% was seen at a cut-off of 0 pg/ml (0.00 micrograms/l), with specificity of 0%.
- UCHL-1 had an AUC of 0.80. Sensitivity of 100% was seen at a cut-off of 40 pg/ml (0.40 micrograms/l), with specificity of 39%.

A prospective cohort study[73] included 1,696 people with head trauma who had blood samples taken before CT, and within 3 hours of injury. Patients' injuries were classified as: concussion, epidural haematoma, subdural haematoma, subarachnoid haemorrhage, brain contusions and brain oedema. Overall 8% of patients had traumatic lesions on CT. S100B levels were significantly higher. Cerebral oedema was associated with significantly higher S100B levels than the other types of injury. Significantly higher S100B levels were seen with 3 simultaneous lesions than with 1 or 2 lesions. Additionally, the presence of skull or facial fractures was also associated with significantly higher S100B levels.

A validation study[74] included 4,030 people with mild head injury who had S100B levels measured immediately and again 3 hours after injury, compared with CT findings within 6 hours of injury. Two different assays were tested. Cerebral lesions on CT scan were identified with sensitivity 96.3% and negative-predictive value of 99.4% using the Diasorin assay, with 1 incorrect result. The Roche Diagnostics assay had sensitivity of 100% and negative predictive value of 100%, with no incorrect results. S100B reduced rapidly, leading to lower sensitivity and negative predictive value at 3 hours.

A retrospective study[75] included 250 people with traumatic brain injury who had at least 2 radiological investigations and at least 3 blood tests for S100B, with at least one test more than 48 hours after injury. New pathological findings were seen on second imaging in 39% of the sample. And this was highly correlated with increased in S100B of more than 0.05 micrograms/l. A secondary increase of more than 0.05 micrograms/l had sensitivity of 80% and lower specificity of 89%, compared with a secondary increase of more than 0.5 micrograms/l had sensitivity of 16%, and specificity of 98%, to detect secondary radiological findings. The secondary radiological findings were also significantly correlated with outcome.

A prospective observational study[76] included 782 people with mild head injury who were aged older than 65 years or were taking clopidogrel or low-dose aspirin at the time of injury. Blood samples were taken within 3 hours

of trauma. Overall, 6.4% of patients had intracranial bleeding. One patient with positive CT results had an S100B level below 0.105 micrograms/l. Of all patients, 33.1% had S100B values below the cut-off. S100B had sensitivity of 98.0%, specificity of 35.3%, positive predictive value of 9.4%, and negative predictive value of 99.6%.

A prospective cohort study[77] included 209 people with mild or moderate traumatic brain injury and 188 people with trauma without brain injury. Blood samples were obtained within 4 hours of injury and tested for S100B and GFAP. Of 262 people who had head CT, intracranial lesions were seen in 8%. Extracranial fractures were seen in 35% of the general trauma patients. Levels of S100B were significantly higher in patients with fractures, compared with those without fractures whether or not traumatic brain injury was present. However, GFAP levels were not significantly affected by the presence of fractures. The AUC for predicting intracranial lesions on CT was 0.84 for GFAP and was 0.78 for S100B. However, in the presence of extracranial fractures, the AUC increased to 0.93 for GFAP and decreased to 0.75 for S100B.

An analysis[78] included 41 people with minor head injury who had CT, MRI, and S100B testing. MRI detected 10 more lesions than CT. At a cut-off of 1.0 micrograms/l, S100B had sensitivity of 100% and specificity of 25%. Structural brain lesions were associated with significantly higher S100B levels.

*Other biomarkers*

An observational study[79] included 206 people with traumatic brain injury who had blood tests for ubiquitin C-terminal hydrolase L1 (UCHL-1) and glial fibrillary acidic protein (GFAP). Correlation between the 2 biomarkers was weak. UCH-L1 had an AUC of 0.87 and GFAP had an AUC of 0.91 for discriminating between people with traumatic brain injury and healthy controls. The combined use of both biomarkers had an AUC of 0.94. Both biomarkers discriminated between patients with traumatic intracranial lesions on CT and those without such lesions, but GFAP was significantly more sensitive and specific (AUC 0.88 compared with 0.71 for UCH-L1). Neither biomarker had adequate sensitivity and specificity for predicting outcome 3 months after injury.

A systematic review and meta-analysis[80] of 5 observational studies (673 case of traumatic brain injury and 1,004 matched controls) assessed UCHL-1 for detecting traumatic brain injury. Serum UCHL-1 was significantly increased in patients with traumatic brain injury compared with controls.

An analysis of data from the TRACK-TBI study[81] included 215 people with traumatic head injury who underwent CT and had testing for GFAP and breakdown products. Of this cohort, 83% had mild, 4% had moderate and 13% had severe traumatic brain injury, with 54% showing acute traumatic lesions on CT. The AUC was 0.88 for GFAP breakdown product levels identifying patients with traumatic lesions on CT and the optimum cut-off of was 0.68 ng/ml. The AUC was 0.65 for identifying unfavourable outcome at 6 months.

*Biomarkers in children*

A prospective cohort study[82] included 197 children and young people with blunt head trauma and 60 controls with traumatic injury without head trauma who had blood samples obtained within 6 hours of injury. Head CT was performed in 152 children and showed traumatic intracranial lesions in 11%. Median GFAP levels were significantly higher in children with intracranial lesions than those without lesions. The AUC was 0.82 for GFAP detecting traumatic intracranial lesions on CT, and was similar for children presenting with GCS of 15 and in those aged under 5 years. At a cut-off of 0.15 ng/ml, GFAP had sensitivity of 94%, specificity of 47%, and a negative predictive value of 98%.

A prospective cohort study[83] included 114 children with head trauma and 41 with trauma without head injury. Of 92 patients who had head CT, 9% had intracranial lesions. The AUC for distinguishing head trauma from no head trauma was 0.84 for GFAP and 0.64 for S100B. The AUC for predicting intracranial lesions on CT was 0.85 for GFAP and 0.67 for S100B. The AUC for predicting intracranial lesions in children ages 10 years or younger was 0.96 for GFAP and 0.72 for S100B. In children younger than 5 years old, the AUC was 1.00 for GFAP and 0.62 for S100B.

An analysis[84] assessing PECARN plus S100B included 109 children with minor head trauma, 8% of whom had clinically important intracranial injury. The modified PECARN rule, which accounted for S100B results could have avoided 32 unnecessary CTs. S100B was negative in 4 children who were at high risk of head injury according to PECARN, but would

not have been missed by the combined method.

A prospective cohort study[85] assessed S100B for detecting brain injury in 73 children younger than 16 years who underwent CT. Blood was obtained within 6 hours of trauma. Overall, 27.4% of the children had intracranial injury detected by CT. S100B had an AUC of 0.73. At a cut-off of 0.14 micrograms/l, S100B had sensitivity of 95% and specificity of 34% in all children and sensitivity of 100% and specificity of 37% in children aged older than 2 years.

**Topic expert feedback**

Topic expert feedback suggested that the use of biomarkers was of clinical interest.

**Impact statement**

Evidence identified in surveillance is consistent with that assessed by the guideline in finding that biomarkers such as S100B, GFAP, and UCHL-1 generally have high sensitivity but low specificity.

The evidence identified in surveillance also has similar limitations to the evidence evaluated during guideline development including:

- differences in the time from injury to blood sampling,
- the time from blood sampling to laboratory measurement is unclear in the abstracts,
- technical specifications of equipment used to measure the levels of biomarkers within blood may differ between studies,
- the reference cut-off for normal levels of individual biomarkers differs between studies.

Additionally, evidence suggests that defining cut-offs may be problematic. For example age, race and presence of bone fractures had important effects on serum levels of S100B.

Avoiding unnecessary CT is particularly important in children, and evidence for biomarkers in children was also identified. However, this consists of small observational studies and concerns about the limitations of the evidence on adults also applies to the evidence in children.

Overall, the evidence base does not seem to have developed sufficiently since the guideline was published to warrant an update in this area.

New evidence is unlikely to change guideline recommendations.

## 176 – 12 Radiation exposure management

### Recommendations derived from this review question

1.4.6 In line with good radiation exposure practice, make every effort to minimise radiation dose during imaging of the head and cervical spine, while ensuring that image quality and coverage is sufficient to achieve an adequate diagnostic study. [2003]

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

**176 – 13 What are the effects on patient outcomes of providing an immediate CT versus observation?**

### Recommendations derived from this review question

This review question was a sub-question of 176-08, so informed the development of recommendations 1.4.1–1.4.5 (see above).

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## *Investigating injuries to the cervical spine*

**176 – 14 What is the best diagnostic imaging technique to determine which patients have sustained damage to the cervical spine and require further assessment of cervical spine?**

### Recommendations derived from this review question

1.5.1 Be aware that, as a minimum, CT should cover any areas of concern or uncertainty on X-ray or clinical grounds. [2003]

1.5.2 Ensure that facilities are available for multiplanar reformatting and interactive viewing of CT cervical spine scans. [2003, amended 2014]

1.5.3 MR imaging is indicated if there are neurological signs and symptoms referable to the cervical spine. If there is suspicion of vascular injury (for example, vertebral malalignment, a fracture involving the foramina transversaria or lateral processes, or a posterior circulation syndrome), CT or MRI angiography of the neck vessels may be performed to evaluate for this. [2003, amended 2014]

1.5.4 Be aware that MRI may add important information about soft tissue injuries associated with bony injuries demonstrated by X-ray and/or CT. [2003]

1.5.5 MRI has a role in the assessment of ligamentous and disc injuries suggested by X-ray, CT or clinical findings. [2003]

1.5.6 In CT, routinely review on 'bone windows' the occipital condyle region for patients who have sustained a head injury. Reconstruction of standard head images onto a high-resolution bony algorithm is readily achieved with modern CT scanners. [2003]

1.5.7 In patients who have sustained high-energy trauma or are showing signs of lower cranial nerve palsy, pay particular attention to the region of the foramen magnum. If necessary, perform additional high-resolution imaging for coronal and sagittal reformatting while the patient is on the scanner table. [2003]

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## 176 – 15 What is the best clinical decision rule for selecting adults, infants and children with head injury for initial imaging with plain X-rays or CT scan for cervical spine injury?

### Sub-questions

What is the best clinical decision rule for selecting adults, infants and children with head injury, who have received a negative X-ray of the cervical spine, for further imaging with CT or MR imaging for cervical spine injury?

What is the best clinical decision rule for selecting adults, infants and children with head injury, who have received a negative CT cervical spine scan, for further imaging with MR imaging for cervical spine injury?

### Recommendations derived from this review question

1.5.8 For adults who have sustained a head injury and have any of the following risk factors, perform a CT cervical spine scan within 1 hour of the risk factor being identified:

- GCS less than 13 on initial assessment.
- The patient has been intubated.
- Plain X-rays are technically inadequate (for example, the desired view is unavailable).
- Plain X-rays are suspicious or definitely abnormal.
- A definitive diagnosis of cervical spine injury is needed urgently (for example, before surgery).
- The patient is having other body areas scanned for head injury or multi-region trauma.
- The patient is alert and stable, there is clinical suspicion of cervical spine injury and any of the following apply:
  - age 65 years or older
  - dangerous mechanism of injury (fall from a height of greater than 1 metre or 5 stairs; axial load to the head, for example, diving; high-speed motor vehicle collision; rollover motor accident; ejection from a motor vehicle; accident involving motorised recreational vehicles; bicycle collision)
  - focal peripheral neurological deficit
  - paraesthesia in the upper or lower limbs.

  A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

1.5.9 For adults who have sustained a head injury and have neck pain or tenderness but no indications for a CT cervical spine scan (see recommendation 1.5.8), perform 3-view cervical spine X-rays within 1 hour if either of these risk factors are identified:

- It is not considered safe to assess the range of movement in the neck (see recommendation 1.5.10).
- Safe assessment of range of neck movement shows that the patient cannot actively rotate their neck to 45 degrees to the left and right.

  The X-rays should be reviewed by a clinician trained in their interpretation within 1 hour of being performed. [new 2014]

1.5.10 Be aware that in adults and children who have sustained a head injury and in whom there is clinical suspicion of cervical spine injury, range of movement in the neck can be assessed safely before imaging only if no high-risk factors (see recommendations 1.5.8, 1.5.11 and 1.5.12) and at least 1 of the following low-risk features apply. The patient:

- was involved in a simple rear-end motor vehicle collision
- is comfortable in a sitting position in the emergency department
- has been ambulatory at any time since injury
- has no midline cervical spine tenderness
- presents with delayed onset of neck pain. [new 2014]

1.5.11 For children who have sustained a head injury, perform a CT cervical spine scan only if any of the following apply (because of the increased risk to the thyroid gland from ionising radiation and the generally lower risk of significant spinal injury):

- GCS less than 13 on initial assessment.
- The patient has been intubated.
- Focal peripheral neurological signs.
- Paraesthesia in the upper or lower limbs.
- A definitive diagnosis of cervical spine injury is needed urgently (for example, before surgery).
- The patient is having other body areas scanned for head injury or multi-region trauma.
- There is strong clinical suspicion of injury despite normal X-rays.
- Plain X-rays are technically difficult or inadequate.
- Plain X-rays identify a significant bony injury.

  The scan should be performed within 1 hour of the risk factor being identified. A provisional written radiology report should be made available within 1 hour of the scan being performed. [new 2014]

1.5.12 For children who have sustained a head injury and have neck pain or tenderness but no indications for a CT cervical spine scan (see recommendation 1.5.11), perform 3-view cervical spine X-rays before assessing range of movement in the neck if either of these risk factors are identified:

- Dangerous mechanism of injury (that is, fall from a height of greater than 1 metre or 5 stairs; axial load to the head, for example, diving; high-speed motor vehicle collision; rollover motor accident; ejection from a motor vehicle; accident involving motorised recreational vehicles; bicycle collision).
- Safe assessment of range of movement in the neck is not possible (see recommendation 1.5.10).

  The X-rays should be carried out within 1 hour of the risk factor being identified and reviewed by a clinician trained in their interpretation within 1 hour of being performed. [new 2014]

1.5.13 If range of neck movement can be assessed safely (see recommendation 1.5.10) in a child who has sustained a head injury and has neck pain or tenderness but no indications for a CT cervical spine scan, perform 3-view cervical spine X-rays if the child cannot actively rotate their neck 45 degrees to the left and right. The X-rays should be carried out within 1 hour of this being identified and reviewed by a clinician trained in their interpretation within 1 hour of being performed. [new 2014]

1.5.14 In children who can obey commands and open their mouths, attempt an odontoid peg view. [2003, amended 2014]

## Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

## *Information and support for families and carers*

**176 – 16 Support for families and carers**

### Recommendations derived from this review question

1.6.1 Staff caring for patients with a head injury should introduce themselves to family members or carers and briefly explain what they are doing. [2003, amended 2014]

1.6.2 Ensure that information sheets detailing the nature of head injury and any investigations likely to be used are made available in the emergency department. NICE's information for the public about this guideline may be helpful. [2003]

1.6.3 Staff should consider how best to share information with children and introduce them to the possibility of long-term complex changes in their parent or sibling. Literature produced by patient support groups may be helpful. [2003]

1.6.4 Encourage family members and carers to talk and make physical contact (for example, holding hands) with the patient. However, it is important that relatives and friends do not feel obliged to spend long periods at the bedside. If they wish to stay with the patient, encourage them to take regular breaks. [2003, amended 2007]

1.6.5 Ensure there is a board or area displaying leaflets or contact details for patient support organisations either locally or nationally to enable family members and carers to gather further information. [2003]

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## *Transfer from hospital to a neuroscience unit*

**176 – 17 What are the benefits for patients of receiving treatment at a neurosciences centre who have suffered a clinically important brain injury that does not require surgical intervention?**

### Recommendations derived from this review question

**Transfer of adults**

1.7.1 Local guidelines on the transfer of patients with head injuries should be drawn up between the referring hospital trusts, the neuroscience unit and the local ambulance service, and should recognise that:

- transfer would benefit all patients with serious head injuries (GCS 8 or less) irrespective of the need for neurosurgery
- if transfer of those who do not require neurosurgery is not possible, ongoing liaison with the neuroscience unit over clinical management is essential. [2003, amended 2007]

1.7.2 The possibility of occult extracranial injuries should be considered for adults with multiple injuries, and they should not be transferred to a service that is unable to deal with other aspects of trauma. [2007]

1.7.3 There should be a designated consultant in the referring hospital with responsibility for establishing arrangements for the transfer of patients with head injuries to a neuroscience unit and another consultant at the neuroscience unit with responsibility for establishing

arrangements for communication with referring hospitals and for receipt of patients transferred. [2003]

1.7.4 Patients with head injuries requiring emergency transfer to a neuroscience unit should be accompanied by a doctor with appropriate training and experience in the transfer of patients with acute brain injury. They should be familiar with the pathophysiology of head injury, the drugs and equipment they will use and working in the confines of an ambulance (or helicopter if appropriate). They should have a dedicated and adequately trained assistant. They should be provided with appropriate clothing for the transfer, medical indemnity and personal accident insurance. Patients requiring non-emergency transfer should be accompanied by appropriate clinical staff. [2003, amended 2007]

1.7.5 Provide the transfer team responsible for transferring a patient with a head injury with a means of communicating changes in the patient's status with their base hospital and the neurosurgical unit during the transfer. [2003, amended 2014]

1.7.6 Although it is understood that transfer is often urgent, complete the initial resuscitation and stabilisation of the patient and establish comprehensive monitoring before transfer to avoid complications during the journey. Do not transport a patient with persistent hypotension, despite resuscitation, until the cause of the hypotension has been identified and the patient stabilised. [2003, amended 2007]

1.7.7 Intubate and ventilate all patients with GCS 8 or less requiring transfer to a neuroscience unit, and any patients with the indications detailed in recommendation 1.7.8. [2003]

1.7.8 Intubate and ventilate the patient immediately in the following circumstances:

- Coma – not obeying commands, not speaking, not eye opening (that is, GCS 8 or less).
- Loss of protective laryngeal reflexes.
- Ventilatory insufficiency as judged by blood gases: hypoxaemia ($PaO_2$ < 13 kPa on oxygen) or hypercarbia ($PaCO_2$ > 6 kPa).
- Spontaneous hyperventilation causing $PaCO_2$ < 4 kPa.
- Irregular respirations. [2003, amended 2007]

1.7.9 Use intubation and ventilation before the start of the journey in the following circumstances:

- Significantly deteriorating conscious level (1 or more points on the motor score), even if not coma.
- Unstable fractures of the facial skeleton.
- Copious bleeding into mouth (for example, from skull base fracture).
- Seizures. [2003, amended 2007]

1.7.10 Ventilate an intubated patient with muscle relaxation and appropriate short-acting sedation and analgesia. Aim for a $PaO_2$ greater than 13 kPa, $PaCO_2$ 4.5 to 5.0 kPa unless there is clinical or radiological evidence of raised intracranial pressure, in which case more aggressive hyperventilation is justified. If hyperventilation is used, increase the inspired oxygen concentration. Maintain the mean arterial pressure at 80 mm Hg or more by infusion of fluid and vasopressors as indicated. In children, maintain blood pressure at a level appropriate for the child's age. [2003, amended 2007]

1.7.11 Education, training and audit are crucial to improving standards of transfer; appropriate time and funding for these activities should be provided. [2003]

1.7.12 Give family members and carers as much access to the patient as is practical during transfer. If possible, give them an opportunity to discuss the reasons for transfer and how the transfer process works with a member of the healthcare team. [2003, amended 2014]

**Transfer of children**

1.7.13 Recommendations 1.7.1–1.7.12 were written for adults, but apply these principles equally to children and infants, providing that the paediatric modification of the GCS is used. [2003]

1.7.14 Service provision in the area of paediatric transfer to tertiary care should also follow the principles outlined in the National Service Framework for Paediatric Intensive Care. These do not conflict with the principles outlined in this section. [2003]

1.7.15 The possibility of occult extracranial injuries should be considered for children with multiple injuries. Do not transfer them to a service that is unable to deal with other aspects of trauma. [2007]

1.7.16 Transfer of a child or infant to a specialist neurosurgical unit should be undertaken by staff experienced in the transfer of critically ill children. [2003]

1.7.17 Give family members and carers as much access to their child as is practical during transfer. If possible, give them an opportunity to discuss the reasons for transfer and how the transfer process works with a member of the healthcare team. [2003, amended 2014]

## Surveillance decision

This review question should not be updated.

---

### *Transfer to specialist centres*

**Surveillance summary (2017)**

A systematic review and meta-analysis[86] of 4 cohort studies (n=4,688) assessed secondary transfer to specialist neurosciences centres for people with head injury. The main limitation of the included studies was confounding by indication due to selective transfer of patients with less severe injuries. The overall risk of bias was rated as high for both mortality and disability. Secondary transfer to specialist neuroscience centres was associated with significantly improved mortality. However, no significant association between non-specialist care and poor outcome was seen.

A cohort study[87] (Risk Adjustment In Neurocritical Care; RAIN) included 3,210 people with GCS less than 15 who were admitted to critical care after head injury. It assessed models for predicting risk of acute traumatic brain injury and the cost-effectiveness of critical care in a location with specialist neuroscience services. At 6 months, 81% of people had follow-up data. Of survivors, 44% had severe disability, 30% had moderate disability and 26% had made a good recovery at 6 months. Overall, 61% of patients had an unfavourable outcome (death or severe disability) at 6 months. Between 35% and 70% of survivors reported problems with quality of life (across 5 domains of the EQ-5D-3L). Risk prediction models were reported to fall ''below the level required to guide individual patient decision-making'. The best performing model of 10 studied was the International Mission for Prognosis and Analysis of Clinical Trials in TBI Lab model (IMPACT), but it substantially under-predicted poor outcome at 6 months. Dedicated neurocritical care units had higher mean quality-adjusted life years (QALYs) at greater cost, with an incremental cost-effectiveness ratio (ICER) of £14,000 compared with combined neurological and general critical care units. After adjusting for differences in case-mix, transfer to a neuroscience centre within 18 hours of presentation was associated with higher lifetime QALYs at additional cost with and ICER of £11,000 compared with no transfer or transfer after 24 hours. A further publication[88] of this study, reporting the same results, was also identified.

A registry analysis[89] included 161 patients with traumatic brain injury who had neurosurgical intervention within 300 minutes of the emergency department admission. People with severe injuries in other body regions were excluded. Subdural haematoma was seen in 85.8% of patients, subarachnoid haemorrhage in 55.5%, and equal numbers had epidural haematoma and intraparenchymal haemorrhage at 22.6% for both conditions. Univariate analysis suggested that people who had surgery within 200 minutes had significantly lower mortality than those who had surgery after 200 minutes. This association remained significant after adjusting for clinically important covariates.

**Topic expert feedback**

Topic experts highlighted the RAIN study.

**Impact statement**

Studies generally show benefits of transfer to specialist neuroscience centres. However, confounding by indication may be an issue with observational studies in this area, such that people with the most severe injuries do not undergo transfer.

The RAIN study provides support for the recommendation that all patients with serious traumatic brain injury would benefit from

transfer to a neurosciences centre, regardless of the need for surgery.

RAIN included people with CGS less than 15, but the current recommendation for transfer applies to people with GCS of 8 or lower. However, all patients included in RAIN were admitted to critical care, suggesting that those with mild and moderate head injury had extracranial injuries needing critical care. Early management of complex and severe extracranial injuries is outside of the remit of this guideline.

New evidence is unlikely to change guideline recommendations.

## *Admission and observation*

### 176 – 18 Admission and observation

#### Recommendations derived from this review question

1.8.1 Use the criteria below for admitting patients to hospital following a head injury:

- Patients with new, clinically significant abnormalities on imaging.
- Patients whose GCS has not returned to 15 after imaging, regardless of the imaging results.
- When a patient has indications for CT scanning but this cannot be done within the appropriate period, either because CT is not available or because the patient is not sufficiently cooperative to allow scanning.
- Continuing worrying signs (for example, persistent vomiting, severe headaches) of concern to the clinician.
- Other sources of concern to the clinician (for example, drug or alcohol intoxication, other injuries, shock, suspected non-accidental injury, meningism, cerebrospinal fluid leak). [2003]

1.8.2 Be aware that some patients may require an extended period in a recovery setting because of the use of general anaesthesia during CT imaging. [2003, amended 2007]

1.8.3 Admit patients with multiple injuries under the care of the team that is trained to deal with their most severe and urgent problem. [2003]

1.8.4 In circumstances where a patient with a head injury requires hospital admission, admit the patient only under the care of a team led by a consultant who has been trained in the management of this condition during their higher specialist training. The consultant and their team should have competence (defined by local agreement with the neuroscience unit) in assessment, observation and indications for imaging (see recommendations 1.4.7–1.4.12 and 1.5.8–1.5.14); inpatient management; indications for transfer to a neuroscience unit (see section 1.7); and hospital discharge and follow-up (see section 1.9). [2003, amended 2007]

**Observation of admitted patients**

1.8.5 In-hospital observation of patients with a head injury should only be conducted by professionals competent in the assessment of head injury. [2003]

1.8.6 For patients admitted for head injury observation the minimum acceptable documented neurological observations are: GCS; pupil size and reactivity; limb movements; respiratory rate; heart rate; blood pressure; temperature; blood oxygen saturation. [2003]

1.8.7 Perform and record observations on a half-hourly basis until GCS equal to 15 has been achieved. The minimum frequency of observations for patients with GCS equal to 15 should be as follows, starting after the initial assessment in the emergency department:

- Half-hourly for 2 hours.
- Then 1-hourly for 4 hours.

- Then 2-hourly thereafter. [2003]

1.8.8 Should the patient with GCS equal to 15 deteriorate at any time after the initial 2-hour period, observations should revert to half-hourly and follow the original frequency schedule. [2003]

1.8.9 Any of the following examples of neurological deterioration should prompt urgent reappraisal by the supervising doctor.

- Development of agitation or abnormal behaviour.
- A sustained (that is, for at least 30 minutes) drop of 1 point in GCS score (greater weight should be given to a drop of 1 point in the motor response score of the GCS).
- Any drop of 3 or more points in the eye-opening or verbal response scores of the GCS, or 2 or more points in the motor response score.
- Development of severe or increasing headache or persisting vomiting.
- New or evolving neurological symptoms or signs such as pupil inequality or asymmetry of limb or facial movement. [2003, amended 2007]

1.8.10 To reduce inter-observer variability and unnecessary referrals, a second member of staff competent to perform observation should confirm deterioration before involving the supervising doctor. This confirmation should be carried out immediately. Where a confirmation cannot be performed immediately (for example, no staff member available to perform the second observation) the supervising doctor should be contacted without the confirmation being performed. [2003]

1.8.11 If any of the changes noted in recommendation 1.8.9 are confirmed, an immediate CT scan should be considered, and the patient's clinical condition re assessed and managed appropriately. [2003, amended 2007]

1.8.12 In the case of a patient who has had a normal CT scan but who has not achieved GCS equal to 15 after 24 hours' observation, a further CT scan or MRI scanning should be considered and discussed with the radiology department. [2003]

**Observation of infants and young children**

1.8.13 Observation of infants and young children (that is, aged under 5 years) is a difficult exercise and therefore should only be performed by units with staff experienced in the observation of infants and young children with a head injury. Infants and young children may be observed in normal paediatric observation settings, as long as staff have the appropriate experience. [2003]

**Training in observation**

1.8.14 Medical, nursing and other staff caring for patients with head injury admitted for observation should all be capable of performing the observations listed in recommendations 1.8.6, 1.8.9 and 1.8.10. [2003]

1.8.15 The acquisition and maintenance of observation and recording skills require dedicated training and this should be made available to all relevant staff. [2003]

1.8.16 Specific training is required for the observation of infants and young children. [2003]

## Surveillance decision

This review question should not be updated.

---

### *Observation and repeat CT in children*

**Surveillance summary (2017)**

A retrospective study[90] included 71 children with isolated skull fracture, 22.5% of whom were discharged after evaluation, and the remainder were admitted for observation. None of the patients needed neurosurgical intervention or had repeat head imaging during admission. However, 3 people who were initially admitted re-attended and had further imaging. Age of the patient was not associated with repeat imaging or inpatient observation. Costs were significantly higher in the group admitted to hospital.

A retrospective study[91] assessed 120 children with traumatic brain injury 88% of whom underwent repeat CT. Children who had repeat CT were older and more likely to have epidural haematoma. Children who did not have repeat CT had no worsening of symptoms or need for surgery. Of the children having repeat CT, 6.6% had progression detected, most commonly in children with epidural haematoma.

A retrospective analysis[92] included 118 children (aged 18 years and younger) with mild traumatic brain injury. Of this cohort, 69 children had repeat imaging, and 6 children showed haemorrhagic progression. Overall, 8 children had clinically important neurological deterioration, and 6 children underwent neurosurgery. These outcomes were significantly more common in children with epidural haematoma compared with other types of intracranial haemorrhage.

An analysis of data from a prospective cohort study[93] included 14,983 children younger than 18 years who underwent CT after blunt head trauma, 152 of whom had cerebral contusions. Isolated cerebral contusions were seen in 54 children, and 57.4% of this group had normal mental status. Most (79.6%) were admitted to hospital, with 29.6% admitted to an intensive care unit. No children with isolated cerebral contusions died, were intubated for head trauma for longer than 24 hours, or needed neurosurgery.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

In children admitted for observation after initial CT, evidence suggests that progression of brain injury in children is uncommon. The small possibility of progression, provides some support for current guidance on observation to detect worsening or a lack of expected improvement in signs or symptoms.

New evidence is unlikely to change guideline recommendations.

---

### *Indications for repeat CT in adults*

**Surveillance summary (2017)**

A systematic review and meta-analysis[94] of 41 studies (n=10,501) assessed repeat CT in people with traumatic brain injury. Overall, repeat CT was associated with a change in management in 11.4% of people in 13 prospective studies and 9.6% of people in 28 retrospective studies. In subgroup analysis of mild brain injury, repeat CT was associated with a change in management in 2.3% of people in 5 prospective studies and 3.9% of people in 9 retrospective studies. The authors concluded that further studies in the area are needed.

A prospective cohort study[95] included 1,129 people with traumatic intracranial haemorrhage, 1,099 of whom had repeat CT. Progression was seen in 216 patients, with 4 people needing neurological intervention. Repeat CT was performed because of neurological deterioration in 30 people, 16 of whom had progression on repeat CT, and 12 of those needed neurosurgical intervention. There was an association between neurological deterioration in neurologic examination and need for neurosurgical intervention. The negative predictive value of neurological deterioration in neurologic examination in predicting the need for neurosurgical intervention was 100% in patients with GCS of less than 8.

A retrospective cohort study[96] included 323 people with mild traumatic brain injury on initial and repeat CT who presented within 24 hours of injury. The median time between scans was 6 hours. Four patients died within 2 weeks of injury, 3 of whom had been admitted to hospital on their initial visits, and 1 had been discharged home. Of 206 patients discharged from the emergency department, 28 re-attended within 1 week. Of the 92 who were admitted to hospital, 3 needed neurosurgical intervention.

A retrospective study[97] included 321 people with ‘minimal’ head injury who had a normal neurological examination after 24 hours. Repeat head CT was performed in 44% of this group. No patient had a neurological deterioration or required a neurosurgical intervention. There was no significant difference in the neurological outcomes, mortality, or discharge dispositions between both groups. Patients managed without a repeat CT had significantly shorter length of stay in hospital.

No evidence was identified.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

The available evidence suggests that repeat CT may be useful for influencing management of people with traumatic brain injury, particularly if neurological status deteriorates. There does not appear to be a need for repeat CT if clinical status does not indicate deterioration or lack of improvement, which is consistent with current recommendations.

New evidence is unlikely to change guideline recommendations.

## *Discharge and follow-up*

### 176 – 19 Discharging patients

#### Recommendations derived from this review question

**Discharge criteria**

1.9.1 If CT is not indicated on the basis of history and examination the clinician may conclude that the risk of clinically important brain injury to the patient is low enough to warrant transfer to the community, as long as no other factors that would warrant a hospital admission are present (for example, drug or alcohol intoxication, other injuries, shock, suspected non-accidental injury, meningism, cerebrospinal fluid leak) and there are appropriate support structures for safe transfer to the community and for subsequent care (for example, competent supervision at home). [2003]

1.9.2 After normal imaging of the head, the clinician may conclude that the risk of clinically important brain injury requiring hospital care is low enough to warrant transfer to the community, as long as the patient has returned to GCS equal to 15, and no other factors that would warrant a hospital admission are present (for example, drug or alcohol intoxication, other injuries, shock, suspected non-accidental injury, meningism, cerebrospinal fluid leak) and there are appropriate support structures for safe transfer to the community and for subsequent care (for example, competent supervision at home). [2003]

1.9.3 After normal imaging of the cervical spine the clinician may conclude that the risk of injury to the cervical spine is low enough to warrant transfer to the community, as long as the patient has returned to GCS equal to 15 and their clinical examination is normal, and no other factors that would warrant a hospital admission are present (for example, drug or alcohol intoxication, other injuries, shock, suspected non-accidental injury, meningism, cerebrospinal fluid leak) and there are appropriate support structures for safe transfer to the community and for subsequent care (for example, competent supervision at home). [2003]

1.9.4 Do not discharge patients presenting with head injury until they have achieved GCS equal to 15, or normal consciousness in infants and young children as assessed by the paediatric version of the GCS. [2003]

**Discharge of patients with no carer at home**

1.9.5 All patients with any degree of head injury should only be transferred to their home if it is certain that there is somebody suitable at home to supervise the patient. Discharge patients with no carer at home only if suitable supervision arrangements have been organised, or when the risk of late complications is deemed negligible. [2003]

**Discharge after observation**

1.9.6 Patients admitted after a head injury may be discharged after resolution of all significant symptoms and signs providing they have suitable supervision arrangements at home. [2003]

### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## 176 – 20 What information and support do patients with head injury say they want?

### Sub-question

What discharge information should be given to patients with head injury?

### Recommendations derived from this review question

1.9.7 Give verbal and printed discharge advice to patients with any degree of head injury who are discharged from an emergency department or observation ward, and their families and carers. Follow recommendations in Patient experience in adult NHS services [NICE clinical guideline 138] about providing information in an accessible format. [new 2014]

1.9.8 Printed advice for patients, families and carers should be age-appropriate and include:

- Details of the nature and severity of the injury.
- Risk factors that mean patients need to return to the emergency department (see recommendations 1.1.4 and 1.1.5).
- A specification that a responsible adult should stay with the patient for the first 24 hours after their injury.
- Details about the recovery process, including the fact that some patients may appear to make a quick recovery but later experience difficulties or complications.
- Contact details of community and hospital services in case of delayed complications.
- Information about return to everyday activities, including school, work, sports and driving.
- Details of support organisations. [new 2014]

1.9.9 Offer information and advice on alcohol or drug misuse to patients who presented to the emergency department with drug or alcohol intoxication when they are fit for discharge. [2003]

1.9.10 Inform patients and their families and carers about the possibility of persistent or delayed symptoms following head injury and whom to contact if they experience ongoing problems. [new 2014]

1.9.11 For all patients who have attended the emergency department with a head injury, write to their GP within 48 hours of discharge, giving details of clinical history and examination. This letter should also be shared with health visitors (for pre-school children) and school nurses (for school-age children). If appropriate, provide a copy of the letter for the patient and their family or carer. [new 2014]

### Surveillance decision

This review question should not be updated.

---

*Text message follow-up*

**Surveillance summary (2017)**

A pilot RCT[98] included 43 people with mild traumatic brain injury who received 14 days' of text message-based education and support for post-concussion symptoms. The abstract did not report the number of participants in the control group, only that test-messaging support was not provided to this group. People who received text message education and had lower odds of reporting headache, difficulty concentrating, and irritability or anxiety. Mean scores for headaches, difficulty concentrating and irritability or anxiety were not significantly improved with text message support.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

Evidence suggests that text messaging may be a useful tool for providing education and support to people with recent mild traumatic brain injury. However, the small sample size in this study, and that it was referred to by its authors as a pilot study, means that it is unlikely to be sufficient to inform recommendations in this area.

New evidence is unlikely to change guideline recommendations.

---

## 176 – 21 The best tool for identifying the patients who should be referred to rehabilitation services following the initial management of a head injury

### Recommendations derived from this review question

No recommendations were made for this review question. A research recommendation was made (see RR – 05 later in this document).

### Surveillance decision

This review question should not be updated.

---

**Surveillance summary (2017)**

A study[99] (n=485) validated existing tools for predicting poor outcome after mild traumatic brain injury. Patient data from adults in a pilot observational study (TRACK-TBI) were used to validate the prognostic models. One prognostic model was from the CRASH study and the other was from researchers in Nijmegen, The Netherlands. The authors concluded that both models had poor performance (AUC 0.49 to 0.56) for predicting outcome at 3 months and 6 months.

A study[100] (n=3,063) assessed a tool for predicting persistent post-concussive symptoms in children and young people.

The derivation cohort (n=2,006) had an AUC of 0.71 (95% CI 0.69 to 0.74) and the validation cohort had an AUC of 0.68 (95% CI 0.65 to 0.72). The authors concluded that their risk score had modest discrimination for risk of persistent post-concussive symptoms.

**Topic expert feedback**

Topic experts highlighted the study by Zemek et al. (2016).[100]

**Impact statement**

Evidence suggests that methods for predicting the occurrence of persistent symptoms after concussion do not have sufficient performance to support their use.

New evidence is unlikely to change guideline recommendations.

---

### 176 – 22 Follow-up

#### Recommendations derived from this review question

1.9.12 When a patient who has undergone imaging of the head and/or been admitted to hospital experiences persisting problems, ensure that there is an opportunity available for referral from primary care to an outpatient appointment with a professional trained in assessment and management of sequelae of brain injury (for example, clinical psychologist, neurologist, neurosurgeon, specialist in rehabilitation medicine). [2003]

#### Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

---

## Editorial and factual corrections identified during surveillance

During surveillance editorial or factual corrections were identified.

- An editorial correction is needed to include a cross-reference in recommendation 1.2.8 to the more recent guideline on major trauma (NICE NG39), which has recommendations on volume resuscitation in people with traumatic brain injury and haemorrhagic shock.
- An editorial correction is needed to include a cross-reference in recommendation 1.4.12 to the more recent guideline on blood transfusion (NICE NG24), which has recommendations on reversal of warfarin anticoagulation in people with suspected traumatic intracranial haemorrhage.

## Research recommendations

### *Prioritised research recommendations*

At pre-specified surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. We may then propose to remove research recommendations from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full versions of the guideline. See NICE's research recommendations process and methods guide 2015 for more information.

These research recommendations were deemed priority areas for research by the Guideline Committee; therefore, at this surveillance review time point a decision **will** be taken on whether to retain the research recommendations or stand them down.

We applied the following approach:

- New evidence relevant to the research recommendation was found and an update of the related review question is planned.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database. If needed, a new research recommendation may be made as part of the update process.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.
  - The research recommendation will be retained because there is evidence of research activity in this area.

- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database because further research is unlikely to impact on the guideline.
- Ongoing research relevant to the research recommendation was found.
  - The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.
- No new evidence relevant to the research recommendation was found and no ongoing studies were identified.
  - The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.
- The research recommendation would be answered by a study design that was not included in the search (usually systematic reviews or randomised controlled trials).
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.
- The research recommendation was made during a recent update of the guideline.
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

### RR – 01 Is the clinical outcome of patients with head injury with a reduced level of consciousness improved by direct transport from the scene of injury to a tertiary centre with neuroscience facilities compared with the outcome of those who are transported initially to the nearest hospital without neurosurgical facilities?

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Evidence on transfer to neuroscience centres was identified, in particular the HITS-NS study, which is directly relevant to this research recommendation. However, transfer to specialist centres has not been shown to be effective in increasing good outcomes. Furthermore, trauma services have been undergoing changes such that patients with life-threatening injuries should generally be taken to major trauma centres, which should have neurosurgical facilities onsite. This has reduced the relevance of this research recommendation.

#### Surveillance decision

The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database because further research is unlikely to impact on the guideline.

### RR – 02 What is the clinical and cost effectiveness of the 2014 NICE guideline recommendation on CT head scanning versus clinical decision rules including CHALICE, CATCH and PECARN for selection of children and infants for head CT scan?

The new research recommendation was made during a recent update of the guideline.

Although new evidence on decision rules for children was found, no studies evaluated the 2014 NICE guideline.

### Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

**RR – 03 In patients with head injury does the use of antiplatelet and anticoagulant drugs increase the risk of intracranial haemorrhage over and above factors included in the current recommendations for CT head scans?**

The research recommendation was made during a recent update of the guideline.

Although new evidence on antiplatelet and anticoagulant drugs was found, it does not fully answer this research recommendation. The guideline committee reporting data similar to that from the AHEAD study. The AHEAD study was included in the evidence on antiplatelet and anticoagulant drugs.

### Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

**RR – 04 In adults with medium risk indications for brain injury under current NICE CT head injury guidance, what is the clinical and cost effectiveness of using the diagnostic circulating biomarker S100B to rule out significant intracranial injury?**

The new research recommendation was made during a recent update of the guideline.

Although new evidence on biomarkers was found, it does not fully answer this research recommendation.

### Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

**RR – 05 Research is needed to summarise and identify the optimal predictor variables for long-term sequelae following mild traumatic brain injury. A systematic review of the literature could be used to derive a clinical decision rule to identify relevant patients at the time of injury. This would in turn lay the foundation for a derivation cohort study.**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

### Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

## *Other research recommendations*

The following research recommendations were not deemed as priority areas for research by the guideline committee.

**RR – 06 Research is needed to develop consensus on criteria for lesions not currently considered to be surgically significant following imaging of a patient with head injury.**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Evidence on early or late neurosurgery was identified, in particular the STITCH study, which is directly relevant to this research recommendation. However, insufficient statistical power due to low recruitment means that the results cannot inform new recommendations in this area.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

### RR – 07 What is the clinical and cost effectiveness of the NICE guideline recommendation on CT head scanning in this update versus other clinical decision rules (including the Scandinavian and NCWFNS) for selection of patients for CT head scan?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Although new evidence assessing clinical decision rules was found, none of the studies compared the diagnostic accuracy of any clinical decision rule with NICE's 2014 recommendations on indications for CT.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

### RR – 08 In children and infants with suspected cervical spine injury, are any existing clinical decision rules for selection of patients for cervical spine imaging clinically and cost effective in the UK NHS?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

### RR – 09 Do patients with significant traumatic brain injury who do not require operative neurosurgical intervention at presentation, but are still cared for in specialist neurosciences centres, have improved clinical outcomes when compared to similar patients who are treated in non-specialist centres?

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

The RAIN study, which is relevant to this research recommendation found that transfer to specialist neuroscience centres is cost effective, which supports current recommendations.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

## References


1. Burrows P, Trefan L, Houston R et al. (2015) Head injury from falls in children younger than 6 years of age. Archives of Disease in Childhood 100:1032-1037.
2. Chen HH, Hsu CC, Weng SF et al. (2015) Hemodialysis with end-stage renal disease did not raise the risk of intracranial hemorrhage after a head injury. Scandinavian Journal of Trauma, Resuscitation & Emergency Medicine 23:82.
3. Sauter TC, Kreher J, Ricklin ME et al. (2015) Risk Factors for Intracranial Haemorrhage in Accidents Associated with the Shower or Bathtub. PLoS ONE [Electronic Resource] 10:e0141812.
4. Ahmadi K, Hashemian AM, Pishbin E et al. (2014) The role of headache management in minor head injury before performing brain CT scan - can intravenous morphine sulfate predict intracranial injury? Ulusal Travma ve Acil Cerrahi Dergisi 20:432-436.
5. Shams V, S, Morteza B et al. (2014) Comparison of paracetamol (apotel) and morphine in reducing post pure head trauma headache. Anesthesiology & Pain Medicine 4:e14903.
6. Rowell SE, Fair KA, Barbosa RR et al. (2016) The impact of pre-hospital administration of lactated ringer's solution versus normal saline in patients with traumatic brain injury. Journal of Neurotrauma 33:1054-1059.
7. Bossers SM, Schwarte LA, Loer SA et al. (2015) Experience in Prehospital Endotracheal Intubation Significantly Influences Mortality of Patients with Severe Traumatic Brain Injury: A Systematic Review and Meta-Analysis. PLoS ONE [Electronic Resource] 10:e0141034.
8. Karamanos E, Talving P, Skiada D et al. (2014) Is prehospital endotracheal intubation associated with improved outcomes in isolated severe head injury? A matched cohort analysis. Prehospital & Disaster Medicine 29:32-36.
9. Sobuwa S, Hartzenberg HB, Geduld H et al. (2013) Outcomes following prehospital airway management in severe traumatic brain injury. South African Medical Journal 103:644-646.
10. Newgard CD, Meier EN, Bulger EM et al. (2015) Revisiting the "Golden Hour": An Evaluation of Out-of-Hospital Time in Shock and Traumatic Brain Injury. Annals of Emergency Medicine 66:30-41, 41.
11. Wang HE, Brown SP, MacDonald RD et al. (2014) Association of out-of-hospital advanced airway management with outcomes after traumatic brain injury and hemorrhagic shock in the ROC hypertonic saline trial. Emergency Medicine Journal 31:186-191.
12. Vavilala MS, Kernic MA, Wang J et al. (2014) Acute care clinical indicators associated with discharge outcomes in children with severe traumatic brain injury. Critical Care Medicine 42:2258-2266.
13. Garner AA, Mann KP, Fearnside M et al. (2015) The Head Injury Retrieval Trial (HIRT): a single-centre randomised controlled trial of physician prehospital management of severe blunt head injury compared with management by paramedics only. Emergency Medicine Journal 32:869-875.
14. Pickering A, Cooper K, Harnan S et al. (2015) Impact of prehospital transfer strategies in major trauma and head injury: systematic review, meta-analysis, and recommendations for study design. The Journal of Trauma and Acute Care Surgery 78:164-177.
15. Lecky F, Russell W, Fuller G et al. (2016) The Head Injury Transportation Straight to Neurosurgery (HITS-NS) randomised trial: a feasibility study. Health Technology Assessment (Winchester, England) 20:1-198.
16. Fuller G, Lawrence T, Woodford M et al. (2015) Emergency medical services interval and mortality in significant head injury: a retrospective cohort study. European Journal of Emergency Medicine 22:42-48.
17. Fuller G, McClelland G, Lawrence T et al. (2016) The diagnostic accuracy of the HITSNS prehospital triage rule for identifying patients with significant traumatic brain injury: a cohort study. European Journal of Emergency Medicine 23:61-64.
18. Fuller G, Lawrence T, Woodford M et al. (2014) The accuracy of alternative triage rules for identification of significant traumatic brain injury: a diagnostic cohort study. Emergency Medicine Journal 31:914-919.

19. Gregson BA, Rowan EN, Francis R et al. (2015) Surgical Trial In Traumatic intraCerebral Haemorrhage (STITCH): a randomised controlled trial of Early Surgery compared with Initial Conservative Treatment. Health Technology Assessment (Winchester, England) 19:1-138.

20. Mendelow AD, Gregson BA, Rowan EN et al. (2015) Early Surgery versus Initial Conservative Treatment in Patients with Traumatic Intracerebral Hemorrhage (STITCH[Trauma]): The First Randomized Trial. Journal of Neurotrauma 32:1312-1323.

21. Zhang K, Jiang W, Ma T et al. (2016) Comparison of early and late decompressive craniectomy on the long-term outcome in patients with moderate and severe traumatic brain injury: A meta-analysis. British Journal of Neurosurgery 30:251-257.

22. Joseph B, Aziz H, Sadoun M et al. (2013) The acute care surgery model: managing traumatic brain injury without an inpatient neurosurgical consultation. The Journal of Trauma and Acute Care Surgery 75:102-105.

23. Culotta PA, Crowe JE, Tran QA et al. (2016) Performance of computed tomography of the head to evaluate for skull fractures in infants with suspected non-accidental trauma. Pediatric Radiology 1-8.

24. Langford S, Panigrahy A, Narayanan S et al. (2015) Multiplanar reconstructed CT images increased depiction of intracranial hemorrhages in pediatric head trauma. Neuroradiology 57:1263-1268.

25. Rabiner JE, Friedman LM, Khine H et al. (2013) Accuracy of point-of-care ultrasound for diagnosis of skull fractures in children. Pediatrics 131:e1757-e1764.

26. Mehta H, Acharya J, Mohan AL et al. (2016) Minimizing Radiation Exposure in Evaluation of Pediatric Head Trauma: Use of Rapid MR Imaging. Ajnr: American Journal of Neuroradiology 37:11-18.

27. Lim D, Lee SH, Kim DH et al. (2014) The possibility of application of spiral brain computed tomography to traumatic brain injury. American Journal of Emergency Medicine 32:1051-1054.

28. Prichep LS, Naunheim R, Bazarian J et al. (2015) Identification of hematomas in mild traumatic brain injury using an index of quantitative brain electrical activity. Journal of Neurotrauma 32:17-22.

29. Ayaz S, I, Thomas C, Kulek A et al. (2015) Comparison of quantitative EEG to current clinical decision rules for head CT use in acute mild traumatic brain injury in the ED. American Journal of Emergency Medicine 33:493-496.

30. Lo WS, Shih YN, Leung CS et al. (2016) A retrospective study of patients with minor head injury to compare the canadian CT head rule and the new orleans criteria. Hong Kong Journal of Emergency Medicine 23:25-33.

31. Borgialli DA, Hoyle JD, Powell EC et al. (2016) Performance of the Pediatric Glasgow Coma Scale Score in the Evaluation of Children With Blunt Head Trauma. Academic Emergency Medicine 23:878-884.

32. Daymont C, Klassen TP, Osmond MH et al. (2015) Accuracy of physician-estimated probability of brain injury in children with minor head trauma. Canadian Journal of Emergency Medicine 17:387-394.

33. Easter JS, Bakes K, Dhaliwal J et al. (2014) Comparison of PECARN, CATCH, and CHALICE rules for children with minor head injury: a prospective cohort study. Annals of Emergency Medicine 64:145-52, 152.

34. Gravel J, Gouin S, Chalut D et al. (2015) Derivation and validation of a clinical decision rule to identify young children with skull fracture following isolated head trauma. CMAJ Canadian Medical Association Journal 187:1202-1208.

35. Kocyigit A, Serinken M, Ceven Z et al. (2014) A strategy to optimize CT use in children with mild blunt head trauma utilizing clinical risk stratification; could we improve CT use in children with mild head injury? Clinical Imaging 38:236-240.

36. Dayan PS, Holmes JF, Atabaki S et al. (2014) Association of traumatic brain injuries with vomiting in children with blunt head trauma. Annals of Emergency Medicine 63:657-665.

37. Dayan PS, Holmes JF, Hoyle J et al. (2015) Headache in traumatic brain injuries from blunt head trauma. Pediatrics 135:504-512.

38. Lee LK, Monroe D, Bachman MC et al. (2014) Isolated loss of consciousness in children with minor blunt head trauma. JAMA Pediatrics 168:837-843.

39. Nishijima DK, Holmes JF, Dayan PS et al. (2015) Association of a Guardian's Report of a Child Acting Abnormally With Traumatic Brain Injury After Minor Blunt Head Trauma. JAMA Pediatrics 169:1141-1147.

40. Ip IK, Raja AS, Gupta A et al. (2015) Impact of clinical decision support on head computed tomography use in patients with mild traumatic brain injury in the ED. American Journal of Emergency Medicine 33:320-325.

41. Dhandapani S, Sarda AC, Kapoor A et al. (2015) Validation of a New Clinico-Radiological Grading for Compound Head Injury: Implications on the Prognosis and the Need for Surgical Intervention. World Neurosurgery 84:1244-1250.

42. Idil H, Kirimli G, Korol G et al. (2015) Are emergency physicians competent to interpret the cranial CT of patients younger than the age of 2 years with mild head trauma? American Journal of Emergency Medicine 33:1175-1177.

43. Mason S, Kuczawski M, Teare MD et al. (13-1-2017) AHEAD Study: an observational study of the management of anticoagulated patients who suffer head injury. BMJ Open 7:e014324.

44. Kuczawski M, Stevenson M, Goodacre S et al. (13-12-2016) Should all anticoagulated patients with head injury receive a CT scan? Decision-analysis modelling of an observational cohort. BMJ.Open 6:e013742.

45. Beynon C, Potzy A, Sakowitz OW et al. (2015) Rivaroxaban and intracranial haemorrhage after mild traumatic brain injury: A dangerous combination? Clinical Neurology & Neurosurgery 136:73-78.

46. Chauny JM, Marquis M, Bernard F et al. (2016) Risk of Delayed Intracranial Hemorrhage in Anticoagulated Patients with Mild Traumatic Brain Injury: Systematic Review and Meta-Analysis. Journal of Emergency Medicine 26:26.

47. Docimo S, Jr, Demin A et al. (2014) Patients with blunt head trauma on anticoagulation and antiplatelet medications: can they be safely discharged after a normal initial cranial computed tomography scan? American Surgeon 80:610-613.

48. Huynh TK, Costello JL, and Rebuck JA. (2014) Optimizing the dose of three-factor prothrombin complex concentrate in traumatic brain injury patients on warfarin therapy. Pharmacotherapy:The Journal of Human Pharmacology & Drug Therapy 34:260-264.

49. Lim BL, Manauis C, and Asinas-Tan ML. (2016) Outcomes of warfarinized patients with minor head injury and normal initial CT scan. American Journal of Emergency Medicine 34:75-78.

50. Albrecht JS, Liu X, Baumgarten M et al. (2014) Benefits and risks of anticoagulation resumption following traumatic brain injury. JAMA Internal Medicine 174:1244-1251.

51. van dB, C L, Tolido T et al. (2016) Systematic Review and Meta-Analysis: Is Pre-Injury Antiplatelet Therapy Associated with Traumatic Intracranial Hemorrhage? Journal of Neurotrauma 9:9.

52. Leong LB and David TK. (2015) Is Platelet Transfusion Effective in Patients Taking Antiplatelet Agents Who Suffer an Intracranial Hemorrhage? Journal of Emergency Medicine 49:561-572.

53. Joseph B, Pandit V, Aziz H et al. (2014) Clinical outcomes in traumatic brain injury patients on preinjury clopidogrel: a prospective analysis. The Journal of Trauma and Acute Care Surgery 76:817-820.

54. Joseph B, Aziz H, Pandit V et al. (2014) Low-dose aspirin therapy is not a reason for repeating head computed tomographic scans in traumatic brain injury: a prospective study. Journal of Surgical Research 186:287-291.

55. Joseph B, Pandit V, Meyer D et al. (2014) The significance of platelet count in traumatic brain injury patients on antiplatelet therapy. The Journal of Trauma and Acute Care Surgery 77:417-421.

56. Dunham CM, Hoffman DA, Huang GS et al. (2014) Traumatic intracranial hemorrhage correlates with preinjury brain atrophy, but not with antithrombotic agent use: a retrospective study. PLoS ONE [Electronic Resource] 9:e109473.

57. Grandhi R, Harrison G, Voronovich Z et al. (2015) Preinjury warfarin, but not antiplatelet medications, increases mortality in elderly traumatic brain injury patients. The Journal of Trauma and Acute Care Surgery 78:614-621.

58. Joseph B, Sadoun M, Aziz H et al. (2014) Repeat head computed tomography in anticoagulated traumatic brain injury patients: still warranted. American Surgeon 80:43-47.

59. McCammack KC, Sadler C, Guo Y et al. (2015) Routine repeat head CT may not be indicated in patients on anticoagulant/antiplatelet therapy following mild traumatic brain injury. The Western Journal of Emergency Medicine 16:43-49.

60. Nishijima DK, Shahlaie K, Sarkar K et al. (2013) Risk of unfavorable long-term outcome in older adults with traumatic intracranial hemorrhage and anticoagulant or antiplatelet use. American Journal of Emergency Medicine 31:1244-1247.

61. Zangbar B, Pandit V, Rhee P et al. (2015) Clinical outcomes in patients on preinjury ibuprofen with traumatic brain injury. American Journal of Surgery 209:921-926.

62. Yuan Q, Sun YR, Wu X et al. (2016) Coagulopathy in Traumatic Brain Injury and Its Correlation with Progressive Hemorrhagic Injury: A Systematic Review and Meta-Analysis. Journal of Neurotrauma 33:1279-1291.

63. Folkerson LE, Sloan D, Cotton BA et al. (2015) Predicting progressive hemorrhagic injury from isolated traumatic brain injury and coagulation. Surgery 158:655-661.

64. Raj R, Siironen J, Kivisaari R et al. (2013) External validation of the international mission for prognosis and analysis of clinical trials model and the role of markers of coagulation. Neurosurgery 73:305-311.

65. Yuan Q, Wu X, Du ZY et al. (2015) Low-dose recombinant factor VIIa for reversing coagulopathy in patients with isolated traumatic brain injury. Journal of Critical Care 30:116-120.

66. Joseph B, Aziz H, Zangbar B et al. (2014) Acquired coagulopathy of traumatic brain injury defined by routine laboratory tests: which laboratory values matter? The Journal of Trauma and Acute Care Surgery 76:121-125.

67. Wu X, Du Z, Yu J et al. (2014) Activity of factor VII in patients with isolated blunt traumatic brain injury: association with coagulopathy and progressive hemorrhagic injury. The Journal of Trauma and Acute Care Surgery 76:114-120.

68. Abdelmalik PA, Boorman DW, Tracy J et al. (2016) Acute Traumatic Coagulopathy Accompanying Isolated Traumatic Brain Injury is Associated with Worse Long-Term Functional and Cognitive Outcomes. Neurocritical Care 24:361-370.

69. Epstein DS, Mitra B, Cameron PA et al. (2016) Normalization of coagulopathy is associated with improved outcome after isolated traumatic brain injury. Journal of Clinical Neuroscience 29:64-69.

70. Heidari K, Vafaee A, Rastekenari AM et al. (2015) S100B protein as a screening tool for computed tomography findings after mild traumatic brain injury: Systematic review and meta-analysis. Brain Injury 29:1146-1157.

71. Bazarian JJ, Blyth BJ, He H et al. (2013) Classification accuracy of serum Apo A-I and S100B for the diagnosis of mild traumatic brain injury and prediction of abnormal initial head computed tomography scan. Journal of Neurotrauma 30:1747-1754.

72. Welch RD, Ayaz S, I, Lewis LM et al. (2016) Ability of serum glial fibrillary acidic protein, ubiquitin C-Terminal Hydrolase-L1, and S100B to differentiate normal and abnormal head computed tomography findings in patients with suspected mild or moderate traumatic brain injury. Journal of Neurotrauma 33:203-214.

73. Wolf H, Frantal S, Pajenda G et al. (2015) Analysis of S100 calcium binding protein B serum levels in different types of traumatic intracranial lesions. Journal of Neurotrauma 32:23-27.

74. Laribi S, Kansao J, Borderie D et al. (2014) S100B blood level measurement to exclude cerebral lesions after minor head injury: the multicenter STIC-S100 French study. Clinical Chemistry & Laboratory Medicine 52:527-536.

75. Thelin EP, Nelson DW, and Bellander BM. (2014) Secondary peaks of S100B in serum relate to subsequent radiological pathology in traumatic brain injury. Neurocritical Care 20:217-229.

76. Thaler HW, Schmidsfeld J, Pusch M et al. (2015) Evaluation of S100B in the diagnosis of suspected intracranial hemorrhage after minor head injury in patients who are receiving platelet aggregation inhibitors and in patients 65 years of age and older. Journal of Neurosurgery 123:1202-1208.

77. Papa L, Silvestri S, Brophy GM et al. (2014) GFAP out-performs S100beta in detecting traumatic intracranial lesions on computed tomography in trauma patients with mild traumatic brain injury and those with extracranial lesions. Journal of Neurotrauma 31:1815-1822.

78. Linsenmaier U, Wirth S, Kanz KG et al. (2016) Imaging minor head injury (MHI) in emergency radiology: MRI highlights additional intracranial findings after measurement of trauma biomarker S-100B in patients with normal CCT. British Journal of Radiology 89:20150827.

79. Diaz-Arrastia R, Wang KK, Papa L et al. (2014) Acute biomarkers of traumatic brain injury: relationship between plasma levels of ubiquitin C-terminal hydrolase-L1 and glial fibrillary acidic protein. Journal of Neurotrauma 31:19-25.

80. Li J, Yu C, Sun Y et al. (2015) Serum ubiquitin C-terminal hydrolase L1 as a biomarker for traumatic brain injury: a systematic review and meta-analysis. American Journal of Emergency Medicine 33:1191-1196.

81. Okonkwo DO, Yue JK, Puccio AM et al. (2013) GFAP-BDP as an acute diagnostic marker in traumatic brain injury: results from the prospective transforming research and clinical knowledge in traumatic brain injury study. Journal of Neurotrauma 30:1490-1497.

82. Papa L, Zonfrillo MR, Ramirez J et al. (2015) Performance of Glial Fibrillary Acidic Protein in Detecting Traumatic Intracranial Lesions on Computed Tomography in Children and Youth With Mild Head Trauma. Academic Emergency Medicine 22:1274-1282.

83. Papa L, Mittal MK, Ramirez J et al. (2016) In Children and Youth with Mild and Moderate Traumatic Brain Injury, Glial Fibrillary Acidic Protein Out-Performs S100beta in Detecting Traumatic Intracranial Lesions on Computed Tomography. Journal of Neurotrauma 33:58-64.

84. Simon-Pimmel J, Lorton F, Guiziou N et al. (2015) Serum S100beta Neuroprotein Reduces Use of Cranial Computed Tomography in Children After Minor Head Trauma. Shock 44:410-416.

85. Manzano S, Holzinger IB, Kellenberger CJ et al. (2016) Diagnostic performance of S100B protein serum measurement in detecting intracranial injury in children with mild head trauma. Emergency Medicine Journal 33:42-46.

86. Fuller G, Pallot D, Coats T et al. (2014) The effectiveness of specialist neuroscience care in severe traumatic brain injury: a systematic review. British Journal of Neurosurgery 28:452-460.

87. Harrison DA, Prabhu G, Grieve R et al. (2013) Risk Adjustment In Neurocritical care (RAIN) - prospective validation of risk prediction models for adult patients with acute traumatic brain injury to use to evaluate the optimum location and comparative costs of neurocritical care: A cohort study. Health Technology Assessment 17:VII-XVII+1.

88. Grieve R, Sadique Z, Gomes M et al. (2016) An evaluation of the clinical and cost-effectiveness of alternative care locations for critically ill adult patients with acute traumatic brain injury. British Journal of Neurosurgery 30:388-396.

89. Matsushima K, Inaba K, Siboni S et al. (2015) Emergent operation for isolated severe traumatic brain injury: Does time matter? The Journal of Trauma and Acute Care Surgery 79:838-842.

90. Blackwood BP, Bean JF, Sadecki-Lund C et al. (2016) Observation for isolated traumatic skull fractures in the pediatric population: Unnecessary and costly. Journal of Pediatric Surgery 51:654-658.

91. Howe J, Fitzpatrick CM, Lakam DR et al. (2014) Routine repeat brain computed tomography in all children with mild traumatic brain injury may result in unnecessary radiation exposure. The Journal of Trauma and Acute Care Surgery 76:292-295.

92. Greenberg JK, Stoev IT, Park TS et al. (2014) Management of children with mild traumatic brain injury and intracranial hemorrhage. The Journal of Trauma and Acute Care Surgery 76:1089-1095.

93. Varano P, Cabrera K, I, Kuppermann N et al. (2015) Acute outcomes of isolated cerebral contusions in children with Glasgow Coma Scale scores of 14 to 15 after blunt head trauma. The Journal of Trauma and Acute Care Surgery 78:1039-1043.

94. Reljic T, Mahony H, Djulbegovic B et al. (2014) Value of repeat head computed tomography after traumatic brain injury: systematic review and meta-analysis. Journal of Neurotrauma 31:78-98.

95. Joseph B, Aziz H, Pandit V et al. (2014) A three-year prospective study of repeat head computed tomography in patients with traumatic brain injury. Journal of the American College of Surgeons 219:45-51.

96. Kreitzer N, Lyons MS, Hart K et al. (2014) Repeat neuroimaging of mild traumatic brain-injured patients with acute traumatic intracranial hemorrhage: clinical outcomes and radiographic features. Academic Emergency Medicine 21:1083-1091.

97. Nayak N, V, Medina B, Patel K et al. (2013) Neurologic outcome of minimal head injury patients managed with or without a routine repeat head computed tomography. The Journal of Trauma and Acute Care Surgery 75:273-278.

98. Suffoletto B, Wagner AK, Arenth PM et al. (2013) Mobile phone text messaging to assess symptoms after mild traumatic brain injury and provide self-care support: a pilot study. Journal of Head Trauma Rehabilitation 28:302-312.

99. Lingsma HF, Yue JK, Maas AI et al. (15-1-2015) 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. 32:83-94.

100. Zemek R, Barrowman N, Freedman SB et al. (8-3-2016) Clinical Risk Score for Persistent Postconcussion Symptoms Among Children With Acute Concussion in the ED. JAMA. 315:1014-1025.