

Head Injury: assessment and early management

[H] Evidence review for CT, MRI and X-ray of the cervical spine in people with head injury – diagnostic

NICE guideline NG232

Evidence reviews underpinning recommendations 1.6.1 to 1.6.11 in the NICE guideline

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Developed by National Institute for Health and Care Excellence

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1 CT, MRI and X-ray of the cervical spine in people with head injury – diagnostic

1.1 Review question

- What is the diagnostic accuracy of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?
- What is the clinical and cost effectiveness of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?

1.1.1 Introduction

Patients with head injury may sustain bony and/or soft tissue injuries to the cervical spine. When imaging is required, the 2014 version of the NICE guideline recommended as the first line test either a series of cervical spine X-rays or a Computerised Tomography (CT) scan. Depending on the clinical situation, Magnetic Resonance (MR) was also indicated in some cases to determine injury to the ligamentous structures, intervertebral discs and spinal cord at both the cranio-cervical junction and the sub-axial cervical spine. This review includes new evidence published since the last update of the guideline on the diagnostic accuracy and clinical and cost effectiveness of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury.

1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question – diagnostic accuracy

Population	Infants, children and adults with head injury and suspected cervical spine injury	
	<u>Strata</u> : C-spine injury risk stratification (based on Canadian C-Spine Rule or National Emergency X-Radiography Utilization Study (NEXUS) criteria – two stratifications are different so to be kept separate)	
	Adults (≥16 years) at: <ul style="list-style-type: none"> • high risk • moderate risk • low risk 	Children + infants (0-16 years) at: <ul style="list-style-type: none"> • high risk • moderate risk • low risk
	Exclusion: adults and children (including infants <1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury.	
	Cut-off of 60% will be used for assigning to strata for all age groups.	
Target condition	Cervical spine injury in patients who have experienced a head injury	
Index tests	<ul style="list-style-type: none"> • Computed tomography (CT) scan of cervical spine • Magnetic resonance imaging (MRI) of cervical spine • X-ray of cervical spine 	
Reference standards	<u>Reference standard for CT</u> : <ul style="list-style-type: none"> • CT and MR imaging of cervical spine Or <ul style="list-style-type: none"> • 2 weeks follow-up after CT including autopsy findings 	
	<u>Reference standard for MR imaging</u> :	

	<ul style="list-style-type: none"> • CT and MR imaging of cervical spine <p>Or</p> <ul style="list-style-type: none"> • 2 weeks follow-up after MR imaging including autopsy findings <p><u>Reference standard for X-ray:</u></p> <ul style="list-style-type: none"> • CT or MR imaging of cervical spine <p>Or</p> <ul style="list-style-type: none"> • CT and MRI imaging of cervical spine <p>Or</p> <ul style="list-style-type: none"> • 2 weeks follow-up after X-ray including autopsy findings <p>For X-ray only include children and people below 65 years.</p> <p>People >65 years are considered as high risk and will be offered CT cervical spine within 8 hours of injury (CG 176).</p> <p>Vascular injuries will be picked up by MR imaging</p>
<p>Statistical measures and outcomes</p>	<p>Diagnostic accuracy CT, MRI and X-ray of the cervical spine for:</p> <ul style="list-style-type: none"> • any significant cervical spine injury <p>(fracture/bony injury, soft tissue/ligament damage, spinal cord injuries, vascular injuries)</p> <p>No objective definition for significant cervical spine injury. Note definitions as reported in the papers.</p> <p>Diagnostic test accuracy to be reported by test <u>sensitivity/specificity</u></p> <p>For measurement of imprecision, clinical decision thresholds for sensitivity and specificity are set at 90% and 60%.</p> <p>Sensitivity is considered to be more important than specificity. Sensitivity is more important as that will change management. Often, the decision is whether someone can be discharged from ED. A test with high sensitivity that is negative is very reassuring in ruling out an injury and allowing early discharge or mobilisation. It's unlikely that imaging will produce false positives.</p>
<p>Study design</p>	<p>Diagnostic cross-sectional studies, cohort studies (prospective and retrospective)</p> <p>Systematic reviews and meta-analyses of the above</p>

Table 2: PICO characteristics of review question – diagnostic test and treat

<p>Population</p>	<p>Infants, children and adults with head injury and suspected cervical spine injury</p> <p><u>Strata:</u> C-spine injury risk stratification (based on Canadian C-Spine Rule or National Emergency X-Radiography Utilization Study (NEXUS) criteria – two stratifications are different so to be kept separate)</p> <table border="1" data-bbox="523 1809 1493 1984"> <tr> <td data-bbox="523 1809 986 1984"> <p>Adults (≥16 years) at:</p> <ul style="list-style-type: none"> • high risk • moderate risk • low risk </td> <td data-bbox="986 1809 1493 1984"> <p>Children + infants (0-16 years) at:</p> <ul style="list-style-type: none"> • high risk • moderate risk • low risk </td> </tr> </table>		<p>Adults (≥16 years) at:</p> <ul style="list-style-type: none"> • high risk • moderate risk • low risk 	<p>Children + infants (0-16 years) at:</p> <ul style="list-style-type: none"> • high risk • moderate risk • low risk
<p>Adults (≥16 years) at:</p> <ul style="list-style-type: none"> • high risk • moderate risk • low risk 	<p>Children + infants (0-16 years) at:</p> <ul style="list-style-type: none"> • high risk • moderate risk • low risk 			

	<p>Exclusion: adults and children (including infants <1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury.</p> <p>Cut-off of 60% will be used for assigning to strata for all age groups.</p>
Target condition	Cervical spine injury in patients who have experienced a head injury
Interventions	<ul style="list-style-type: none"> • Computed tomography (CT) scan of cervical spine • Magnetic resonance imaging (MRI) of cervical spine • X-ray of cervical spine
Comparators	<p>MRI of cervical spine, X-ray of cervical spine and CT of cervical spine compared to each other</p> <p>For X-ray only include children and people below 65 years</p> <p>People >65 years are considered as high risk and will be offered CT cervical spine within 8 hours of injury (CG 176)</p> <p>Vascular injuries will be picked up by MR imaging</p>
Outcomes	<p>All outcomes are considered equally important for decision making and therefore have all been rated as critical:</p> <ul style="list-style-type: none"> • Mortality at 3 months • Quality of life - 3 months or more • Objectively applied score of disability e.g. Glasgow Outcome Score (GOS) or extended GOS - at 3 months or more • Length of hospital stay • Unscheduled re-admission (28 days or longer) • Neurological deterioration <p>Neurological deterioration could be because of either no imaging or no appropriate imaging</p> <p>Spinal injuries are determined by different scales– e.g. American Spinal Injury Association (ASIA), functional independence measure (FIM). Different scales are used. Report as in the studies.</p> <p>Vascular insult would be picked up in outcome neurological deterioration</p>
Study design	<ul style="list-style-type: none"> • Randomised controlled trials (RCTs), systematic reviews of RCTs. • If no RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders, starting with prospective cohort studies. <p>Key confounders</p> <ul style="list-style-type: none"> • Age • Gender • Glasgow Coma Scale (GCS) or pupillary response at presentation

1.1.3 Methods and process

This evidence review was developed using the methods and process described in [Developing NICE guidelines: the manual](#). Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

1.1.4 Diagnostic evidence

1.1.4.1 Included studies

Diagnostic accuracy

Forty-one studies reporting diagnostic accuracy data were included in the review;^{1-7, 9, 10, 12-14, 16-19, 21, 22, 25-31, 33, 35-44, 46-49} these are summarised in Tables 2 and 3 below. Evidence from these studies is summarised in the clinical evidence summary below in Tables 9-23 and references provided in References . The assessment of the evidence quality was conducted with emphasis on test sensitivity and specificity as this was identified by the committee as the primary measure in guiding decision-making. Clinical decision thresholds of sensitivity/specificity =0.9 and 0.60 above which a test would be recommended and 0.7 and 0.4 below which a test is of no clinical use were set by the committee.

Studies focusing on adults and children were reported separately. A total of 33 and 8 studies were identified for adult and children populations, respectively. Some studies evaluated the diagnostic accuracy of more than one diagnostic imaging modality. The number of studies identified for each index test is given below

Adults

- X-ray as index test – 13 studies
- CT as index test – 16 studies
- CT and MRI as separate index tests – 9 studies

Note that the bottom grouping was separated from other studies as these were studies where CT + MRI used as reference standard (or data available to analyse in this way), meaning only sensitivity values could be obtained (no information about specificity given both tests form part of the reference standard).

Children

- X-ray as index test – 3 studies
- CT as index test – 7 studies
- MRI as index test – 6 studies

Population

Head injury

For most studies identified in the literature search, head injury was not mentioned and the population was described only as those with suspected cervical spine injury undergoing imaging of the cervical spine. Despite it being unclear if head injury was present or the proportion that had suffered head injury in these studies, these studies were included and downgraded for indirectness, as it was noted that many of those with cervical spine injury are likely to have experienced head injury based on the nature of the injury, for example those with whiplash are likely to have suffered a head injury as well. For studies where the population was limited to those that were unconscious or obtunded, often requiring intensive care unit admission, although head injury was not specifically mentioned in many studies, it was assumed that these groups did have at least suspected head injury given the severity of their injuries; these studies were not downgraded based on head injury not being mentioned.

However, they were still downgraded for another reason: the severe nature of their injuries makes them a very specific subgroup of the population that attend the emergency department with suspected cervical spine injury. Results would be less applicable than those of people who are discharged from the emergency department without admission to hospital or intensive care.

Therefore, the population of included studies varies, with the following major groups identified:

- Studies where it is clearly stated or suggested (for example undergoing a head CT) that all or a majority of patients sustained a head injury and underwent imaging of the cervical spine
- Studies where the presence of head injury is not mentioned and patients underwent imaging of the cervical spine (for those that were obtunded or unconscious, based on the severity of injuries head injury was assumed to have occurred)
- Studies where it is clear a proportion had some form of confirmed or suspected head injury but for the remaining patients it is unclear (for example, a proportion had head CT or diagnosed with intracranial haemorrhage) and underwent imaging of the cervical spine

The inclusion of studies where it was unclear if head injury was present or not meant that there was overlap with an evidence review relating to cervical spine assessment performed as part of the [NICE Spinal injury: assessment and initial management guideline](#):

- For adults, 13 of the included studies had also been included in the spinal injury assessment and initial management NICE guideline
- For children, 3 of the included studies had also been included in the spinal injury assessment and initial management NICE guideline

Other population details

Some studies included a broad population of patients with suspected cervical spine injury undergoing imaging but others were more specific. For example, some studies only included those that were unconscious or those with severe traumatic injuries. This was taken into account when deciding whether studies were similar enough to be grouped together.

For adults, four main groupings were identified, which are presented in separate included studies tables in [section 1.1.5](#) and separate GRADE tables in [section 1.1.6](#):

- all having index test and not limited to those that were admitted
- only including those admitted, not those subsequently discharged following index test
- only including those that are obtunded, unconscious and/or requiring intensive care unit admission (X-ray was excluded as an index test in this group given X-ray would not be used as the initial imaging test in this population with severe injuries)
- other very specific populations

For children, two main groupings were identified, which are presented in separate included studies tables in [section 1.1.5](#) and separate GRADE tables in [section 1.1.6](#):

- all having index test and not limited to those that were admitted
- only including those that are obtunded, unconscious and/or requiring intensive care unit admission

Reference standards

Reference standards used varied across studies even for those using the same index test. Broad groups of reference standards identified in studies were as follows, though the details may differ between studies:

- **Final diagnosis based on all available information, including additional where performed** – used as a reference standard across X-ray, CT and MRI index test. Diagnosis at discharge often mentioned, some mentioning readmissions, often unclear how long follow-up/time to discharge was and therefore whether follow-up duration matches protocol.
- **CT scan or MRI** – accepted as a reference standard where X-ray was the index test. CT scan often used as the reference standard for bony/osseous injuries (for example, fracture) and MRI for ligamentous injuries. CT also accepted as a reference standard for studies that were assessing the ability of MRI to specifically detect fractures and MRI accepted as a reference standard for studies that were assessing the ability of CT to detect ligamentous injuries, as it was acknowledged that CT would be the reference standard for bony injuries and MRI for ligamentous/soft tissue injuries.
- **CT + MRI combined** – some studies used CT and MRI combined as a reference standard, or provided data that enabled this to be worked out, meaning the sensitivity of CT and MRI individually could be calculated (no information about specificity could be obtained using this as a reference standard for CT and MRI individually as index tests)

Outcome definitions

Target conditions being detected by index tests varied across studies. The protocol for this review specified ‘any significant cervical spine injury’.

Some studies did report only more serious or significant injuries, for example cervical spine injuries that were defined as unstable or requiring intervention.

Some studies only reported ‘any cervical spine injury’, the definition of which varied across studies and was sometimes poorly defined. For studies where this was the only outcome reported, this was accepted and included in the analysis.

Some studies reported both significant injuries and any injuries – in this case the results for significant injuries were included in the analysis as this was more in line with the protocol.

A further way in which outcome definitions varied across studies was the types of injuries (for example, bony or ligamentous/soft tissue) that were included. Some studies included any type of injury in the outcome/target condition whereas others focused the study on specific types of injuries, for example only fractures or only ligamentous injuries.

Pooling

Given the wide variation discussed above in terms of population, reference standard and outcome definitions, pooling of results was not appropriate. Studies that were broadly similar in terms of index test, population, reference standard and target condition were grouped under the same headings but not formally pooled.

Diagnostic test and treat

All included studies provided data for the diagnostic accuracy component of this question, as no diagnostic test and treat studies matching the protocol were identified.

See also the study selection flow chart in Appendix C, sensitivity and specificity forest plots in Appendix E, and study evidence tables in 0.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix I.

1.1.5 Summary of studies included in the diagnostic evidence

Table 3: Summary of studies included in the evidence review – adults – all having index test and not limited to those that were admitted

Study	Population	Target condition	Index test	Reference standard	Comments
X-ray as index test					
<p>Bailitz 2009³</p> <p>N=1505</p> <p>Conducted in USA</p> <p>Prospective</p>	<p>Adults (≥16 years) meeting one or more of NEXUS criteria and requiring cervical spine imaging following trauma</p> <p>Unclear if all or most had head injury as no details provided</p>	<p>Clinically significant cervical spine injury</p>	<p>Cervical spine radiographs (X-ray)</p>	<p>Final diagnosis in medical record at discharge</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: meeting at least one NEXUS criterion – separate results for high, moderate and low risk</p>
<p>Duane 2010¹³</p> <p>N=49</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Adult patients (≥18 years) following blunt trauma who had flexion-extension plain films and MRI of cervical spine</p> <p>Unclear if all or most had head injury as no details provided</p>	<p>Ligamentous injury of the cervical spine</p>	<p>X-ray – flexion-extension plain films</p>	<p>MRI – gold standard for ligamentous injuries</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Focuses only on ligamentous injuries

FINAL
Imaging of the cervical spine

Study	Population	Target condition	Index test	Reference standard	Comments
					<p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
<p>Gale 2005¹⁹</p> <p>N=400</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Blunt trauma patients undergoing head CT and also having plain radiography (X-ray) of cervical spine</p> <p>All included patients underwent head CT</p>	Cervical spine fracture	Plain radiography (X-ray)	CT of cervical spine – gold standard for fractures	<p>Indirectness:</p> <ul style="list-style-type: none"> Focuses only on fractures in the outcome <p>Risk stratification: unclear</p>
<p>Gharekhanloo 2021²⁰</p> <p>N=220</p> <p>Conducted in Iran</p> <p>Prospective</p>	<p>Adult trauma patients referred to an ED in Iran. They received plain radiography and CT to evaluate cervical spine injury.</p> <p>Low risk status based on NEXUS criteria.</p>	Cervical spine injury	Plain radiography (X-ray)	CT of cervical spine – gold standard for cervical spine injury	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear how many had head injury Only 10 people had abnormal CT. <p>Risk stratification: unclear</p>
<p>Griffen 2003²²</p> <p>N=1199</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Adult blunt trauma patients undergoing cervical spine assessment by X ray and CT</p> <p>Unclear if all or most had head injury as no details provided</p>	Cervical spine injury – poorly defined	X-ray of cervical spine	Unclear, possibly all imaging/follow-up	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Unclear if reference standard included a 2-week follow-up period

FINAL
Imaging of the cervical spine

Study	Population	Target condition	Index test	Reference standard	Comments
					<p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
<p>Lee 2001²⁹</p> <p>N=604</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Adult trauma patients undergoing imaging examination of the cervical spine with conventional radiography and helical CT</p> <p>Unclear if all or most had head injury as no details provided</p>	Fractures	Conventional radiography (X-ray)	Helical CT scan	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Focuses only on fractures • Results reported at fracture-level not patient-level (patients could have more than one fracture and these included in analysis individually) <p>Included in spinal assessment guideline</p> <p>Risk stratification: described as high index of suspicion for cervical spine injury (unclear which rule based on)</p>
<p>Mathen 2007³¹</p> <p>N=667</p> <p>Conducted in USA</p>	Trauma patients (average age 35.4 years) not meeting NEXUS low-risk criteria and undergoing CT and	Clinically significant cervical spine injury – requiring surgery or long-term stabilisation with a collar or halo	Plain films (X-ray)	Final diagnosis of cervical spine injury based on all prospectively collected clinical data and imaging results	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury

FINAL
Imaging of the cervical spine

Study	Population	Target condition	Index test	Reference standard	Comments
Prospective	radiography of cervical spine Unclear if all or most had head injury as no details provided				<ul style="list-style-type: none"> Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: those not meeting NEXUS low risk criteria</p>
Nguyen 2005 ³³ N=112 Conducted in USA Prospective	Patients with blunt trauma undergoing imaging of cervical spine Unclear if all or most had head injury as no details provided	Cervical spine fractures	X-ray	Diagnosis based on final reports including all imaging	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Focuses only on fractures Unclear if reference standard included a 2-week follow-up period <p>Risk stratification: reports data for low and high risk separately, based on NEXUS</p>
Takami 2014 ⁴⁶ N=179 Conducted in Japan	Patients sustaining high-energy trauma immobilised and undergoing X-ray and CT of cervical spine	Cervical spine fracture	X-ray of cervical spine	Full CT of spine	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury present in a small proportion but unclear if remaining had head injury as

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Imaging of the cervical spine

Study	Population	Target condition	Index test	Reference standard	Comments
Prospective	Proportion had concomitant head injury but unclear how many, reported to be 15% in those with fractures				<p>part of the injury mechanism</p> <ul style="list-style-type: none"> • Focuses only on fractures <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear, those with high-energy trauma</p>
CT as index test					
<p>Bailitz 2009³</p> <p>N=1505</p> <p>Conducted in USA</p> <p>Prospective</p>	<p>Adults (≥16 years) meeting one or more of NEXUS criteria and requiring cervical spine imaging following trauma</p> <p>Unclear if all or most had head injury as no details provided</p>	Clinically significant cervical spine injury	CT of cervical spine	Final diagnosis in medical record at discharge	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: meeting at least one NEXUS criterion – separate results for high, moderate and low risk</p>
Duane 2016 ¹⁶	Adults (≥18 years) following trauma and	Fracture and/or ligamentous injury	CT scan	Later found to have cervical spine injury –	Indirectness:

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Imaging of the cervical spine

Study	Population	Target condition	Index test	Reference standard	Comments
<p>N=9227</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>undergoing assessment of cervical spine</p> <p>Unclear if most or all had head injury as no details provided</p>			<p>poorly defined. Possibly includes any report of injury during follow-up and also results of any additional imaging performed (e.g. MRI).</p> <p>Likely that reference standard differs between patients and unclear follow-up duration</p>	<ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Reference standard poorly defined and unclear if matches protocol <p>Risk stratification: unclear, described as patients with criteria for trauma team alert</p>
<p>Griffen 2003²²</p> <p>N=1199</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Adult blunt trauma patients undergoing cervical spine assessment by X ray and CT</p> <p>Unclear if all or most had head injury as no details provided</p>	<p>Cervical spine injury – poorly defined</p>	<p>CT of cervical spine</p>	<p>Unclear, possibly all imaging/follow-up</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
<p>Inaba 2016²⁷</p> <p>N=10,276</p> <p>Conducted in USA</p>	<p>Adults (≥18 years) following blunt trauma undergoing CT scan of the cervical spine (failed NEXUS low-risk criteria)</p>	<p>Clinically significant cervical spine fracture</p> <p>Defined as abnormal or equivocal finding on CT or MRI consistent with acute traumatic injury</p>	<p>CT of cervical spine</p>	<p>Final diagnosis at time of discharge, including any additional imaging and operative findings dependent on each patient</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury

Study	Population	Target condition	Index test	Reference standard	Comments
Prospective	Unclear if all or most had head injury as no details provided	along with one of three active interventions: surgical stabilisation, Halo Orthotic placement or use of Cervical-Thoracic Orthotic			<ul style="list-style-type: none"> Limits only to cervical spine fractures Reference standard does not include a 2 week follow-up <p>Risk stratification: patients failing low-risk NEXUS criteria</p>
Mathen 2007 ³¹ N=667 Conducted in USA Prospective	Trauma patients (average age 35.4 years) not meeting NEXUS low-risk criteria and undergoing CT and radiography of cervical spine Unclear if all or most had head injury as no details provided	Clinically significant cervical spine injury – requiring surgery or long-term stabilisation with a collar or halo	Multi-slice CT of cervical spine	Final diagnosis of cervical spine injury based on all prospectively collected clinical data and imaging results	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: those not meeting NEXUS low risk criteria</p>
Nguyen 2005 ³³ N=112 analysed by CT Conducted in USA Prospective	Patients with blunt trauma undergoing imaging of cervical spine Unclear if all or most had head injury as no details provided	Cervical spine fractures	CT of cervical spine	Diagnosis based on final reports including all imaging	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Focuses only on fractures

Study	Population	Target condition	Index test	Reference standard	Comments
					<ul style="list-style-type: none"> Unclear if reference standard included a 2-week follow-up period <p>Risk stratification: reports data for low and high risk separately, based on NEXUS</p>
<p>Ptak 2001³⁷</p> <p>N=676</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Patients (mean age 47.2 years) presenting to emergency radiology division for cervical spine injury evaluation following trauma by CT</p> <p>Unclear if all or most had head injury as no details provided</p>	Cervical spine fracture	CT of cervical spine	Final clinical diagnosis (including operative and discharge), possibly incorporating CT results	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Focuses only on fractures Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
<p>Vanguri 2014⁴⁸</p> <p>N=5676</p>	Adult blunt trauma undergoing cervical spine assessment by CT	Cervical spine injury – poorly defined	Cervical spine CT	Unclear, possibly including other imaging such as MRI and flexion-extension depending on patient	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury

Study	Population	Target condition	Index test	Reference standard	Comments
Conducted in USA Retrospective	Unclear if all or most had head injury as no details provided				<ul style="list-style-type: none"> Unclear if reference standard included a 2-week follow-up period <p>Risk stratification: unclear, those meeting criteria for trauma team activation</p>
CT alone and MRI alone as separate index tests – CT and MRI combined used as reference standard (only sensitivity could be calculated for each of CT and MRI separately)					
Friesen 2014 ¹⁸ N=206 analysed Conducted in Australia Retrospective	Adults (≥16 years) with CT and MRI performed for suspected blunt acute cervical spine trauma Likely most had a suspicion of head injury as 76% had combined cervical spine and brain CT	Unstable cervical spine injury Defined by Denis 3 column definition as well as any cases requiring urgent (within 5 days) surgery or urgent surgical immobilisation (such as halo-traction ring) and following additional injuries: flexion teardrop fracture, bilateral locked facets, hangman's fracture, Jefferson fracture and Type 2 dens fracture	Helical CT of cervical spine OR MRI of cervical spine	MRI said to be reference standard for unstable injuries in the study which is not the case according to our protocol Data presented in paper therefore analysed using combined CT and MRI as reference standard	Reference standard of MRI alone does not match protocol, but available data analysed using CT and MRI as a combined reference standard (meaning only sensitivity could be calculated, not specificity) Risk stratification: 98% met at least one NEXUS criterion for imaging
Malhotra 2018 ³⁰ N=1080 Conducted in USA	Patients with suspected blunt cervical spine injury that underwent CT of cervical spine followed	Any cervical spine injury, including osseous and ligamentous injuries	CT of cervical spine OR MRI of cervical spine	MRI said to be reference standard for cervical spine injuries in the study which is not the	Indirectness: <ul style="list-style-type: none"> Unclear if all had head injury as no details provided

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Study	Population	Target condition	Index test	Reference standard	Comments
Retrospective	by MRI of cervical spine Unclear if most or all had head injury as no details provided			case according to our protocol Data presented in paper therefore analysed using combined CT and MRI as reference standard	Reference standard of MRI alone does not match protocol, but available data analysed using CT and MRI as a combined reference standard (meaning only sensitivity could be calculated, not specificity) Risk stratification: unclear
Novick 2018 ³⁵ N=241 Conducted in USA Retrospective	Patients (mean age 43.9 years) undergoing both CT and MRI of cervical spine for any reason, with a history of trauma in medical records. Unclear if all or most had head injury – 17% reported to have closed head injury, but unclear for others if head injury was part of the injury mechanism	Cervical spine injuries – ligamentous or bony injury of the cervical vertebral spine, disc injuries, or spinal cord injuries as assessed by imaging	CT of cervical spine OR MRI of cervical spine	CT and MRI as a combined reference standard – means specificity cannot be calculated (as false positives not possible when the index test forms part of the reference standard)	Indirectness: <ul style="list-style-type: none"> 17% reported to have closed head injury but unclear if remaining participants suffered head injury as part of the injury mechanism Not possible to calculate specificity using reference standard as defined in the study Risk stratification: unclear
Schoenfeld 2018 ⁴² N=668	Adults receiving CT and MRI for evaluation of cervical spine injury following trauma	Cervical spine injury – poorly defined	CT of cervical spine OR	No specific reference standard mentioned but possible to calculate sensitivity of CT and MRI using CT + MRI as	Indirectness: <ul style="list-style-type: none"> Unclear if all had head injury as no details provided

Study	Population	Target condition	Index test	Reference standard	Comments
Conducted in USA Retrospective	Unclear if most or all had head injury as no details provided		MRI of cervical spine	reference standard as specified in protocol	Using CT + MRI as reference standard means it is only possible to calculate sensitivity and not specificity Risk stratification: unclear
Songur 2020 ⁴⁴ N=195 Conducted in Turkey Retrospective	Patients (mean age 47.3 years) admitted to ED with diagnosis of blunt cervical spine trauma undergoing CT and MRI of cervical spine Unclear if most or all had head injury as no details provided	Unstable cervical spine injury – Based on neurological status of the patient, degree of spinal canal stenosis and degree of instability. Denis' 1983 definition of single-level ligamentous injury extending to two of three columns.	CT of cervical spine OR MRI of cervical spine	MRI said to be reference standard for cervical spine injuries in the study which is not the case according to our protocol Data presented in paper therefore analysed using combined CT and MRI as reference standard	Indirectness: <ul style="list-style-type: none"> Unclear if all had head injury, but suggests all may have had CT of brain Reference standard of MRI alone does not match protocol, but available data analysed using CT and MRI as a combined reference standard (meaning only sensitivity could be calculated, not specificity) Risk stratification: unclear

Table 4: Summary of studies included in the evidence review – adults – only including those admitted, not those subsequently discharged following index test

Study	Population	Target condition	Index test	Reference standard	Comments
X-ray as index test					

Study	Population	Target condition	Index test	Reference standard	Comments
<p>Cohn 1991⁹</p> <p>N=60</p> <p>Conducted in USA</p> <p>Prospective</p>	<p>Admitted with blunt traumatic injury and evaluated for cervical spine injury by cross-table lateral radiographs (X-ray)</p> <p>50% had head CT as part of diagnostic tests, unclear if remaining patients had some form of head injury as part of the injury mechanism</p>	Acute cervical spine injuries – poorly defined	Cross-table lateral radiographs (X-ray)	Reference standard unclear, possibly a final diagnosis based on any further imaging performed	<p>Indirectness:</p> <ul style="list-style-type: none"> 50% had head CT and unclear if remaining had head injury Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
<p>Duane 2008¹⁴</p> <p>N=1004</p> <p>Conducted in USA</p> <p>Prospective</p>	<p>Alert patients (>16 years) following blunt trauma that underwent lateral cervical spine film (X-ray) and cervical spine CT</p> <p>Unclear if all or most had head injury as no details provided</p>	Cervical spine fracture	Lateral cervical spine film (X-ray)	CT of cervical spine – gold standard for fractures	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury Focuses only on fractures in the outcome <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
CT as index test					
<p>Resnick 2014⁴¹</p> <p>N=830</p> <p>Conducted in USA</p>	Adults (>18 years) that sustained blunt trauma and underwent CT evaluation of the cervical spine	Clinically significant cervical spine injury – those requiring surgical intervention for stabilisation or halo placement, as well as	Multidetector row helical CT	Final diagnosis at time of discharge (including all imaging and operative findings)	<p>Indirectness:</p> <ul style="list-style-type: none"> Head injury not mentioned so unclear if most or all had head injury

Study	Population	Target condition	Index test	Reference standard	Comments
Prospective	Unclear if all or most had head injury as no details provided	unstable injuries requiring a hard collar			<ul style="list-style-type: none"> Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>

Table 5: Summary of studies included in the evidence review – adults – only including those that are obtunded, unconscious and/or requiring intensive care unit admission

Study	Population	Target condition	Index test	Reference standard	Comments
X-ray as index test					
Despite some studies reporting data for X-ray as an index test in this population, these were not included given X-ray would not usually be used as an initial imaging test in this population of obtunded/unconscious patients.					
CT as index test					
Adams 2006 ¹ N=97 Conducted in USA Retrospective	Patients undergoing MRI cervical spine trauma protocol at high risk of axial trauma due to pain, neurological symptoms or obtundation after significant blunt trauma Unclear if all or most had head injury as no details provided	Cervical spine injury – poorly defined	CT of cervical spine	Final diagnosis based on MRI and CT and clinical decision-making of spinal consultants	Indirectness: <ul style="list-style-type: none"> All included were at high-risk/more severely injured which may be less applicable to general population of those attending ED with suspected cervical spine injuryUnclear if reference standard included a 2-week follow-up period

Study	Population	Target condition	Index test	Reference standard	Comments
					<ul style="list-style-type: none"> References standard possibly places focus on MRI results <p>Included in spinal assessment guideline</p> <p>Risk stratification: deemed high risk for axial trauma, unclear which stratification rule used</p>
<p>Berne 1999⁴</p> <p>N=58</p> <p>Conducted in USA</p> <p>Prospective</p>	<p>High-risk blunt trauma patients (age ≥17 years) where spine could not be evaluated clinically (e.g. due to head injury, shock, etc.) and need for CT of another body area and intensive care unit admission</p> <p>53% had associated head injury (intracranial bleed), unclear if remaining suffered some form of head injury as part of the injury mechanism</p>	<p>Unstable cervical spine injury – classified as unstable in consultation with combined neurosurgical-orthopaedic spine service and based on published guidelines</p>	<p>Complete cervical CT</p>	<p>Final diagnosis based on all imaging/studies</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All required ICU admission so represent more severe subgroup of injuries which may be less applicable to general population of those attending ED with suspected cervical spine injury Unclear if reference standard included a 2-week follow-up period <p>Risk stratification: described as high-risk blunt trauma, unclear which stratification rule used</p>
<p>Brohi 2005⁶</p> <p>N=381 analysed for CT</p>	<p>Unconscious intubated trauma patients (median age 34 years for whole cohort)</p>	<p>Unstable cervical spine injury – defined using White and Punjabi system and three-column model of Denis</p>	<p>Helical CT scan of cervical spine</p>	<p>Final diagnosis, including all imaging performed (MRI in some) and follow-up</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were unconscious representing a more

Study	Population	Target condition	Index test	Reference standard	Comments
<p>Conducted in UK</p> <p>Retrospective</p>	<p>Unclear if all or most had head injury as no details provided</p>			<p>through hospital stay to identify missed injuries</p>	<p>severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p> <p>Unclear if reference standard included a 2-week follow-up period</p> <p>Included in spinal assessment guideline</p> <p>Risk stratification: not reported, but all were unconscious, intubated patients</p>
<p>Raza 2013⁴⁰</p> <p>N=53</p> <p>Conducted in UK</p> <p>Retrospective</p>	<p>Adult blunt trauma patients with GCS score ≤ 14 (altered sensorium/obtunded), intoxicated with alcohol or drugs and undergoing CT of cervical spine following trauma</p> <p>Unclear if all or most had head injury as no details provided</p>	<p>Clinically significant cervical spine injury - poorly defined</p>	<p>CT of cervical spine</p>	<p>Final diagnosis of injury at hospital discharge, follow-up appointments or any readmissions</p> <p>Possibly includes >2 weeks follow-up as readmissions and follow-up appointments taken into account</p>	<p>Indirectness: All included had altered sensorium/were obtunded representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p> <p>Risk stratification: unclear</p>

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Study	Population	Target condition	Index test	Reference standard	Comments
Widder 2004 ⁴⁹ N=102 Conducted in Canada Prospective	High-risk severely injured patients (average age 32.0 years) following blunt trauma Unclear if all or most had head injury as no details provided	Cervical spine abnormality – poorly defined	CT of cervical spine	Final diagnosis at discharge and any readmissions Possibly includes >2 weeks follow-up as readmissions taken into account	Indirectness: <ul style="list-style-type: none"> All included were high-risk severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury Risk stratification: high-risk severely injured patients, unclear which stratification rule used
CT alone and MRI alone as separate index tests – CT and MRI combined used as reference standard (only sensitivity could be calculated for each of CT and MRI separately)					
Fisher 2013 ¹⁷ N=277 Conducted in USA Retrospective	Obtunded patients (GCS score <15) following blunt trauma undergoing CT and MRI of cervical spine. Mixture of adults and children, but majority were adults ≥18 years (86%) Unclear if most or all had head injury as no details provided	Clinically significant cervical spine injury CT and MRI scans considered clinically significant if detecting one of the following: ligamentous injury in two adjacent spinal columns, sUBLUXATIONS, cord injury, nerve root injury, disc herniations, and fractures except certain types as specified by NEXUS	CT alone OR MRI alone	CT and MRI as a combined reference standard – means specificity cannot be calculated (as false positives not possible when the index test forms part of the reference standard)	Indirectness: <ul style="list-style-type: none"> All included were obtunded representing more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury Despite calculating sensitivity of the two modalities used alone, the study notes the intention was not to compare the accuracy of CT and MRI as a solo modality but to assess the added value of

Study	Population	Target condition	Index test	Reference standard	Comments
					<p>MRI to more safely clear the cervical spine.</p> <p>Not possible to calculate specificity using reference standard as defined in the study</p> <p>Risk stratification: unclear, all obtunded patients</p>
<p>Lau 2018²⁸</p> <p>N=63</p> <p>Conducted in Singapore</p> <p>Retrospective</p>	<p>Patients suffering blunt traumatic injuries that were mentally obtunded and evaluation of cervical spine using CT and MRI</p> <p>Suggests all may have undergone assessment for brain injuries (limited information)</p>	<p>Cervical spine injuries – poorly defined but appears to include bony and soft tissue injuries</p>	<p>CT scan of cervical spine</p> <p>OR</p> <p>MRI of cervical spine</p>	<p>MRI said to be reference standard for cervical spine injuries in the study which is not the case according to our protocol</p> <p>Data presented in paper therefore analysed using combined CT and MRI as reference standard</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were obtunded representing more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury <p>Reference standard of MRI alone does not match protocol, but available data analysed using CT and MRI as a combined reference standard (meaning only sensitivity could be calculated, not specificity)</p> <p>Risk stratification: unclear, all obtunded patients</p>
<p>Parmar 2018³⁶</p> <p>N=27 analysed</p>	<p>Adult unconscious trauma patients that</p>	<p>Any cervical spine injury</p>	<p>CT of cervical spine</p> <p>OR</p>	<p>MRI said to be reference standard for cervical spine injuries in the</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> Indirectness:

Study	Population	Target condition	Index test	Reference standard	Comments
<p>Conducted in Australia</p> <p>Prospective</p>	<p>had CT and MRI of cervical spine</p> <p>Unclear if most or all had head injury as no details provided</p>		MRI of cervical spine	<p>study which is not the case according to our protocol</p> <p>Data presented in paper therefore analysed using combined CT and MRI as reference standard</p>	<ul style="list-style-type: none"> All included were unconscious representing more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury Reference standard of MRI alone does not match protocol, but available data analysed using CT and MRI as a combined reference standard (meaning only sensitivity could be calculated, not specificity) <p>Risk stratification: unclear, all unconscious requiring mechanical ventilation</p>
<p>Tan 2014⁴⁷</p> <p>N=83</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Obtunded patients with diagnosis of intracranial haemorrhage and undergoing CT and MRI of cervical spine following non-high impact trauma (e.g. ground level falls)</p> <p>All had head injury (intracranial haemorrhage) to be included</p>	Unstable cervical spine injury	<p>CT of cervical spine</p> <p>OR</p> <p>MRI of cervical spine</p>	<p>MRI said to be reference standard for cervical spine injuries in the study which is not the case according to our protocol</p> <p>Data presented in paper therefore analysed using combined CT and MRI as reference standard</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were obtunded representing more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury Reference standard of MRI alone does not match protocol, but available data analysed using CT and MRI as a combined reference standard (meaning only

Study	Population	Target condition	Index test	Reference standard	Comments
					<p>sensitivity could be calculated, not specificity)</p> <p>Risk stratification: unclear, all obtunded patients admitted to ICU with intracranial haemorrhage</p>

Table 6: Summary of studies included in the evidence review – adults – other very specific populations

Study	Population	Target condition	Index test	Reference standard	Comments
X-ray as index test					
<p>Dan Lantsman 2020¹⁰</p> <p>N=129 analysed</p> <p>Conducted in Israel</p> <p>Retrospective</p>	<p>Those (median age 83 years) with radiographic diagnosis of diffuse idiopathic skeletal hyperostosis following low-energy trauma and suspected spinal injury (results provided separately for cervical spine injuries)</p> <p>Unclear if all or most had head injury as no details provided</p>	<p>Acute fracture - those not present in studies prior to the trauma and consisting of a radiographically depicted cortical disruption or impaction of the trabeculae and paravertebral soft tissue infiltration.</p>	<p>X-ray of spine</p> <p>Performed in anterior-posterior and lateral projections.</p>	<p>Whole spine CT (results provided separately for cervical spine injuries)</p> <p>Performed in axial plane on 64-slice machine.</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Limited to very specific population of those that had diffuse idiopathic skeletal hyperostosis which may not be applicable to general population • Only includes fracture in the outcome and not other types of injuries <p>Risk stratification: unclear</p>

Study	Population	Target condition	Index test	Reference standard	Comments
<p>Goodnight 2008²¹</p> <p>N=379</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Adults (≥18 years) following blunt trauma that received CT of cervical spine and follow-up flexion-extension radiographs for continued cervical pain</p> <p>Unclear if all or most had head injury as no details provided</p>	Ligamentous cervical spine injury	X-ray – flexion-extension radiographs	All available evidence, including MRI in some patients	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Those with confirmed fractures were excluded, meaning population may differ from those presenting without any imaging/assessment • Focuses only on ligamentous injuries • Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
CT as index test					
<p>Bush 2016⁷</p> <p>N=632 analysed (intoxicated subgroup)</p> <p>Conducted in USA</p> <p>Prospective</p>	<p>Intoxicated adults (≥18 years) with blunt trauma undergoing CT of the cervical spine</p> <p>Unclear if most or all had head injury as no details provided</p>	Clinically significant cervical spine injury: any injury defined as unstable or potentially unstable injury that required surgical stabilisation or prolonged immobilisation.	CT scan	<p>Cervical spine injury diagnosis at discharge/follow-up: includes composite endpoint, which included MRI findings, operative findings and clinical status at discharge.</p> <p>Components of reference standard likely</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Limited to very specific population of those that are intoxicated • Unclear if reference standard included a 2-week follow-up period

Study	Population	Target condition	Index test	Reference standard	Comments
				differ between patients. Also mentions identification of missed clinically significant injuries from outpatient notes following discharge. Unclear how long this follow up was for and whether the same in all patients.	Risk stratification: unclear, but all intoxicated adults
Goodnight 2008 ²¹ N=379 Conducted in USA Retrospective	Adults (≥18 years) following blunt trauma that received CT of cervical spine and follow-up flexion-extension radiographs for continued cervical pain Unclear if all or most had head injury as no details provided	Ligamentous cervical spine injury	Helical CT of cervical spine	All available evidence, including MRI in some patients	Indirectness: <ul style="list-style-type: none"> • Head injury not mentioned so unclear if most or all had head injury • Those with confirmed fractures were excluded, meaning population may differ from those presenting without any imaging/assessment • Focuses only on ligamentous injuries • Unclear if reference standard included a 2-week follow-up period <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>

Table 7: Summary of studies included in the evidence review – children – all having index test and not limited to those that were admitted

Study	Population	Target condition	Index test	Reference standard	Comments
X-ray as index test					
Rana 2009 ³⁹ N=54 Conducted in USA Retrospective	Paediatric patients (<18 years) following trauma and undergoing cervical spine imaging by plain radiography and CT Unclear if all or most had head injury as no details provided	Cervical spine injury – poorly defined	X-ray	CT Unclear if solely CT or other later imaging findings also included	Indirectness: <ul style="list-style-type: none"> Unclear if all had head injury as no details provided Included in spinal assessment guideline Risk stratification: unclear
Somppi 2018 ⁴³ N=574 (n=495 analysed for X-ray) Conducted in USA Retrospective	Children and adolescents (≤19 years) presenting with possible neck injury Unclear if all or most had head injury – 40% of whole population reported to have had a head CT	Cervical spine injury - ligamentous or osseous injury documented by attending radiologist in their report	X-ray	Follow-up/other imaging? Unclear definition. Mentions the following: to ensure complete identification of spinal cord injuries, medical records for all patients with a negative imaging study (CT or MRI) were reviewed for up to 1 month after the index ED visit to assess for cervical spine pain on ED or outpatient visits to the institution	Indirectness: <ul style="list-style-type: none"> 40% of whole population had head CT but unclear if the remaining participants had head injury as part of the injury mechanism unclear if reference standard matches protocol as poorly defined Risk stratification: unclear
CT as index test					
Derderian 2019 ¹² N=221	Children (median age 9 years) following trauma and undergoing cervical	Clinical instability – defined as those undergoing surgical intervention (spinal	CT scan (any abnormality - stable or unstable injuries used to	Clinical instability (requiring intervention or not) – assume this was	Indirectness: <ul style="list-style-type: none"> clear that a proportion suffered head injury as

Study	Population	Target condition	Index test	Reference standard	Comments
<p>Conducted in USA</p> <p>Retrospective</p>	<p>spine CT and MRI scan</p> <p>Unclear if all or most had head injury – 15.8% reported to have isolated head injury and 66.5% multiorgan injury (unclear if this include head injury)</p>	<p>fusion or halo placement)</p>	<p>calculate diagnostic accuracy data)</p>	<p>ascertained through follow-up of records</p> <p>Follow-up duration unclear</p>	<p>part of the injury but unclear if this was the case for most people in the study</p> <p>Not formally described as a diagnostic accuracy study and no sensitivity etc. reported, but data available to calculate sensitivity and specificity for clinically unstable injuries.</p> <p>Risk stratification: unclear</p>
<p>Henry 2013-2²⁵</p> <p>N=84</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Children (≤18 years) with suspected cervical spine injury following trauma with CT and MRI performed within 48 h</p> <p>Unclear if all or most had head injury.</p>	<p>Soft tissue injuries (compression fractures, soft tissue oedema, ligamentous injury, muscular injury and spinal cord injury) of cervical spine</p>	<p>CT – CT assessed for ability to detect soft tissue injuries</p>	<p>MRI –MRI used as reference standard for soft tissue injuries of cervical spine</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> unclear if all or most experienced some form of head injury as part of the injury mechanism outcome limited to soft tissue injuries only <p>Risk stratification: unclear</p>
<p>Rana 2009³⁹</p> <p>N=254</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Paediatric patients (<18 years) following trauma and undergoing cervical spine imaging by plain radiography and CT</p> <p>Unclear if all or most had head injury as no details provided</p>	<p>Cervical spine injury – poorly defined</p>	<p>CT of cervical spine</p>	<p>Subsequent imaging</p> <p>Unclear if everyone followed up for same duration</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> Unclear if all had head injury as no details provided Unclear if reference standard included a 2-week follow-up period

Study	Population	Target condition	Index test	Reference standard	Comments
					<p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear</p>
<p>Somppi 2018⁴³</p> <p>N=574 (n=130 analysed for CT)</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Children and adolescents (<19 years) presenting with possible neck injury</p> <p>Unclear if all or most had head injury – 40% of whole population reported to have had a head CT</p>	<p>Cervical spine injury - ligamentous or osseous injury documented by attending radiologist in their report</p>	<p>CT</p>	<p>Follow-up/other imaging? Unclear definition. Mentions the following: to ensure complete identification of spinal cord injuries, medical records for all patients with a negative imaging study (CT or MRI) were reviewed for up to 1 month after the index ED visit to assess for cervical spine pain on ED or outpatient visits to the institution</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> 40% of whole population had head CT but unclear if the remaining participants had head injury as part of the injury mechanism unclear if reference standard matches protocol as poorly defined <p>Risk stratification: unclear</p>
MRI as index test					
<p>Derderian 2019¹²</p> <p>N=221</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Children (median age 9 years) following trauma and undergoing cervical spine CT and MRI scan</p> <p>Unclear if all or most had head injury – 15.8% reported to have isolated head injury and 66.5% multiorgan injury</p>	<p>Clinical instability – defined as those undergoing surgical intervention (spinal fusion or halo placement)</p>	<p>MRI scan (any abnormality - stable or unstable injuries used to calculate diagnostic accuracy data)</p>	<p>Clinical instability (requiring intervention or not) – assume this was ascertained through follow-up of records</p> <p>Follow-up duration unclear</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> clear that a proportion suffered head injury as part of the injury but unclear if this was the case for most people in the study <p>Not formally described as a diagnostic accuracy study and no sensitivity etc. reported, but data available to calculate sensitivity and</p>

Study	Population	Target condition	Index test	Reference standard	Comments
	(unclear if this include head injury)				specificity for clinically unstable injuries. Risk stratification: unclear
Henry 2013-1 ²⁶ N=73 Conducted in USA Retrospective	Children (≤18 years) with suspected cervical spine injury that could not be cleared using clinical criteria undergoing MRI-STIR within 48 h	Cervical spine injury with instability – requiring surgical stabilisation: either undergoing surgery or demonstrating signs of instability, pain or neurological compromise during follow-up	MRI with STIR (short T1 inversion recovery) sequence	Follow-up or flexion-extension radiographs: injury requiring surgical intervention or presenting with clinical (significant pain or neurological compromise) or radiographic evidence of instability upon follow-up. Flexion-extension radiographs used to identify false positive findings on MRI. Mean follow-up: 10.0 (18.4 months), range 4 days to 7.6 years	Indirectness: <ul style="list-style-type: none"> unclear if all or most experienced some form of head injury as part of the injury mechanism <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear, those that could not be cleared clinically</p>
Henry 2013-2 ²⁵ N=84 Conducted in USA Retrospective	Children (≤18 years) with suspected cervical spine injury following trauma with CT and MRI performed within 48 h Unclear if all or most had head injury.	Osseous injuries (fractures, locked facets, subluxations and dislocations) of cervical spine	MRI – MRI assessed for ability to detect osseous injuries of cervical spine	CT– CT used as reference standard for osseous injuries of cervical spine	Indirectness: <ul style="list-style-type: none"> unclear if all or most experienced some form of head injury as part of the injury mechanism outcome limited to fractures <p>Risk stratification: unclear</p>
Somppi 2018 ⁴³	Children and adolescents (≤19	Cervical spine injury - ligamentous or osseous	MRI	Follow-up/other imaging? Unclear	Indirectness:

Study	Population	Target condition	Index test	Reference standard	Comments
N=574 (n=21 analysed for MRI) Conducted in USA Retrospective	years) presenting with possible neck injury Unclear if all or most had head injury – 40% of whole population reported to have had a head CT	injury documented by attending radiologist in their report		definition. Mentions the following: to ensure complete identification of spinal cord injuries, medical records for all patients with a negative imaging study (CT or MRI) were reviewed for up to 1 month after the index ED visit to assess for cervical spine pain on ED or outpatient visits to the institution	<ul style="list-style-type: none"> 40% of whole population had head CT but unclear if the remaining participants had head injury as part of the injury mechanism unclear if reference standard matches protocol as poorly defined <p>Risk stratification: unclear</p>

Table 8: Summary of studies included in the evidence review – children – only including those that are obtunded, unconscious and/or requiring intensive care unit admission

Study	Population	Target condition	Index test	Reference standard	Comments
X-ray as index test					
Brockmeyer 2012 ⁵ N=24 Conducted in USA Prospective	Children (<17 years) with severe traumatic injuries admitted to ICU undergoing assessment of cervical spine by X-ray, CT and MRI Unclear if all or most had head injury.	Early cervical spine instability – required surgical correction	X-ray	Clinical outcome/diagnosis of early instability – undergoing surgical correction Follow-up possibly >2 weeks as mentions plain radiographs at follow-up of 3-4 months post-injury	Indirectness: <ul style="list-style-type: none"> All included were severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury <p>Note: only one patient had confirmed early instability in the study</p>

Study	Population	Target condition	Index test	Reference standard	Comments
					<p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear, all comatose with severe traumatic injuries</p>
CT as index test					
<p>Al-Sarheed 2020²</p> <p>N=65</p> <p>Conducted in Saudi Arabia</p> <p>Retrospective</p>	<p>Children (<15 years) with suspected cervical spine injury and that were unconscious</p> <p>Unclear if all or most had head injury – 23.3% with skull fracture and 17.4% with intra/extra-axial brain haemorrhage, smaller proportions with skull/face laceration, brain oedema or brain herniation</p>	<p>Cervical spine injury mandating stabilisation – no further details provided</p>	<p>CT scan</p>	<p>Radiology/clinical examination, including MRI for some where this was performed.</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were unconscious representing more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury unclear if reference standard matches protocol as poorly defined <p>Risk stratification: unclear, all were unconscious and intubated</p>
<p>Brockmeyer 2012⁵</p> <p>N=24</p> <p>Conducted in USA</p>	<p>Children (<17 years) with severe traumatic injuries admitted to ICU undergoing assessment of cervical spine by X-ray, CT and MRI</p>	<p>Early cervical spine instability – required surgical correction</p>	<p>CT of cervical spine</p>	<p>Clinical outcome/diagnosis of early instability – undergoing surgical correction</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were severely injured subgroup which may be less applicable to general population of

Study	Population	Target condition	Index test	Reference standard	Comments
Prospective	Unclear if all or most had head injury.			Follow-up possibly >2 weeks as mentions plain radiographs at follow-up of 3-4 months post-injury	<p>those attending ED with suspected cervical spine injury</p> <p>Note: only one patient had confirmed early instability in the study</p> <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear, all comatose with severe traumatic injuries</p>
<p>Qualls 2015³⁸</p> <p>N=63</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Children (median age 9.6 years) at a children's hospital admitted with severe traumatic brain injury and assessed for cervical spine injury with CT and MRI</p> <p>All had severe traumatic brain injury to be included</p>	Unstable cervical spine injury: resulting in neurological deficit localised to cervical spinal cord, operative stabilisation, halo placement or cervical immobilisation of 3 months of greater	CT alone	<p>CT followed by MRI (CT + MRI) combined</p> <p>Some also had plain radiography of cervical spine and unclear if this also used as part of reference standard for these patients</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury <p>Risk stratification: unclear, all with severe traumatic brain injury</p>
MRI as index test					
<p>Brockmeyer 2012⁵</p> <p>N=24</p>	Children (<17 years) with severe traumatic injuries admitted to ICU undergoing	Early cervical spine instability – required surgical correction	MRI of cervical spine	Clinical outcome/diagnosis of early instability –	Indirectness:

Study	Population	Target condition	Index test	Reference standard	Comments
<p>Conducted in USA</p> <p>Prospective</p>	<p>assessment of cervical spine by X-ray, CT and MRI</p> <p>Unclear if all or most had head injury.</p>			<p>undergoing surgical correction</p> <p>Follow-up possibly >2 weeks as mentions plain radiographs at follow-up of 3-4 months post-injury</p>	<ul style="list-style-type: none"> All included were severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury <p>Note: only one patient had confirmed early instability in the study</p> <p>Included in spinal assessment guideline</p> <p>Risk stratification: unclear, all comatose with severe traumatic injuries</p>
<p>Qualls 2015³⁸</p> <p>N=63</p> <p>Conducted in USA</p> <p>Retrospective</p>	<p>Children (median age 9.6 years) at a children's hospital admitted with severe traumatic brain injury and assessed for cervical spine injury with CT and MRI</p> <p>All had severe traumatic brain injury to be included</p>	<p>Unstable cervical spine injury: resulting in neurological deficit localised to cervical spinal cord, operative stabilisation, halo placement or cervical immobilisation of 3 months of greater</p>	<p>MRI alone</p>	<p>CT followed by MRI (CT + MRI) combined</p> <p>Some also had plain radiography of cervical spine and unclear if this also used as part of reference standard for these patients</p>	<p>Indirectness:</p> <ul style="list-style-type: none"> All included were severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury <p>Risk stratification: unclear, all with severe traumatic brain injury</p>

Study	Population	Target condition	Index test	Reference standard	Comments

See 0 for full evidence tables.

1.1.6 Summary of the diagnostic evidence

The assessment of the evidence quality was conducted with emphasis on test sensitivity and specificity as this was identified by the committee as the primary measure in guiding decision-making. Clinical decision thresholds of sensitivity/specificity =0.9 and 0.60 above which a test would be recommended and 0.7 and 0.4 below which a test is of no clinical use were set. Of sensitivity and specificity, it was agreed that sensitivity is the most important measure as the consequences of missing injuries, particularly those that are found to be clinically significant, may be severe.

Results are separated into the four main population groups identified for adults and two main population groups identified for children (see Diagnostic evidence section above for details), which are presented in separate GRADE tables. Within each GRADE table studies are further separated based on whether or not most had head injury or suspected head injury, the reference standard and the outcome (for example any cervical spine injury is separated from those studies reporting clinically significant injuries and those reporting a specific injury only such as fractures are separated from those covering both osseous and ligamentous cervical spine injuries). Although some studies were similar in terms of population, index test, reference standard and outcome, pooling was not performed given the amount of variation across studies included in the review.

Those where the first column has been highlighted in green indicate studies where all or most were thought to have concomitant head injury. Note this does not include those that were in obtunded, unconscious or severely injured populations where we have assumed head injury was present based on the nature of the injuries.

Adults – all having index test and not limited to those that were admitted

Table 9: Clinical evidence summary: X-ray

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Those with blunt trauma with all having head CT, CT as reference standard, cervical spine fracture as outcome												
Gale 2005 Risk stratification: unclear	1	400	CT of cervical spine	Unclear	Cervical spine fracture – no further details	0.32 (0.13 to 0.57)	0.99 (0.98 to 1.00)	Sensitivity				
								Very serious ^a	Serious ^b	None	None	VERY LOW
								Specificity				
								Very serious ^a	Serious ^b	None	None	VERY LOW
Those with trauma and low risk (one NEXUS criterion), unclear if head injury, CT as reference standard, clinically significant cervical spine injury as outcome												
Gharekhanloo 2021	1	220	CT of cervical spine	Unclear	Clinically significant cervical spine injury (based on neurological recommendation for subluxation/dislocation or acute fracture or both)	0.40 (0.12 to 0.74)	0.97 (0.94 to 0.99)	Sensitivity				
								Very serious ^a	Serious ^c	None	Serious ^d	VERY LOW
								Specificity				
								Very serious ^a	Serious ^c	None	None	VERY LOW

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Those meeting at least one NEXUS criterion, unclear if head injury, final diagnosis as reference standard, clinically significant injury as outcome												
Bailitz 2009 – high risk	1	Unclear (n=15 positive on reference standard)	Final diagnosis in medical record at discharge	Unclear	Clinically significant cervical spine injury – requiring operative procedure, halo application and/or rigid cervical collar	0.47 (0.21 to 0.73)	NR	Sensitivity				
								Very serious ^a	Very serious ^c	None	Serious ^d	VERY LOW
								Specificity NA				
Bailitz 2009 – moderate risk	1	Unclear (n=19 positive on reference standard)	Final diagnosis in medical record at discharge	Unclear	Clinically significant cervical spine injury – requiring operative procedure, halo application and/or rigid cervical collar	0.37 (0.16 to 0.62)	NR	Sensitivity				
								Very serious ^a	Very serious ^c	None	None	VERY LOW
								Specificity NA				
Bailitz 2009 – low risk	1	Unclear (n=16 positive on	Final diagnosis in medical	Unclear	Clinically significant cervical spine	0.25 (0.07 to 0.52)	NR	Sensitivity				
								Very serious ^a	Very serious ^c	None	None	VERY LOW
								Specificity NA				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
		reference standard)	record at discharge		injury – requiring operative procedure, halo application and/or rigid cervical collar			Specificity NA				
Mathen 2007	1	667	Final diagnosis based on all prospectively collected clinical data and imaging results	Unclear	Clinically significant cervical spine injury – requiring surgery or long-term stabilisation with a collar or halo	0.44 (0.25 to 0.65)	0.95 (0.93 to 0.97)	Sensitivity				
Risk stratification: those not meeting NEXUS low risk criteria								Very serious ^a	Very serious ^c	None	None	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^c	None	None	VERY LOW
Any following trauma, unclear if head injury, CT as reference standard, cervical spine fractures as outcome												
Lee 2001	1	604 patients (gives results for total	Helical CT scan	Unclear	Cervical spine fracture – no further details	0.33 (0.19 to 0.51)	NR	Sensitivity				
Risk stratification								Very serious ^a	Very serious ^e	None	None	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
tion: described as high index of suspicion for cervical spine injury (unclear which rule based on)		fracture not patients – including some with multiple fractures)						NA				
Takami 2014	1	179	Full CT of spine	Unclear, same admission	Cervical spine fracture – no further details	0.63 (0.35 to 0.85)	NR	Sensitivity				
Risk stratification: unclear, those with high-energy trauma								Very serious ^a	Very serious ^f	None	Serious ^d	VERY LOW
								Specificity				
								NA				
Any with blunt trauma, unclear if head injury, MRI as reference standard, ligamentous cervical spine injury as outcome												
Duane 2010	1	49	MRI of cervical spine	Unclear	Ligamentous cervical	0.00 (0.00 to 0.37)	0.98 (0.87 to 1.00)	Sensitivity				
								Very serious ^a	Very serious ^g	None	None	VERY LOW

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear					spine injury	Of 8 injuries missed, 5 were significant (2 with associated fractures requiring prolonged collar and 3 requiring operation)		Specificity				
								Very serious ^a	Very serious ^g	None	None	VERY LOW
Any with blunt injury and cervical spine assessed, unclear if head injury, reference standard unclear/final diagnosis, cervical spine injuries as outcome												
Griffen 2003 Risk stratification: unclear	1	1199	Unclear, possible all imaging/follow-up	Unclear	Cervical spine injury - poorly defined	0.65 (0.55 to 0.73)	NR	Sensitivity				
								Very serious ^a	Very serious ^c	None	Serious ^d	VERY LOW
								Specificity				
					NA							
Any with blunt injury and cervical spine assessment, unclear if head injury, reference standard unclear/final diagnosis, cervical spine fractures as outcome												
Nguyen 2005 – high risk	1	19	Diagnosis based on final reports including all imaging	Unclear	Cervical spine fractures – no further details	0.93 (0.68 to 1.00)	0.95 (0.74 to 1.00)	Sensitivity				
								Very serious ^a	Very serious ^h	None	Serious ^d	VERY LOW
								Specificity				
					Very serious ^a Very serious ^h None None VERY LOW							
	1	78	Diagnosis based	Unclear	Cervical spine	Not estimable as there were no	1.00 (0.95 to 1.00)	Sensitivity				
								NA				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Nguyen 2005 – low risk			on final reports including all imaging		fractures – no further details	reference standard positive in this low-risk group		Specificity Very serious ^a	Very serious ^h	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unclear if the index test and/or reference standard were interpreted without knowledge of the other, the time interval between index test and reference standard was unclear and it was unclear if the reference standard consisted of the same components for all patients or there was likely to be a difference in components between patients

^b Downgraded by 1 increment as outcome limited to fractures rather than any cervical spine injury

^c Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard included a 2 week follow-up period

^d Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^e Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, outcome limited to fractures rather than any cervical spine injury, and results interpreted at fracture level not patient level (patients could have more than one fracture and these included individually in analysis)

^f Downgraded by 2 increments as head injury mentioned for a small proportion of participants but unclear if head injury was part of the injury mechanism for all or most, and outcome focuses specifically on fractures rather than any cervical spine injury

^g Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and outcome limited to ligamentous injuries rather than any cervical spine injury

^h Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, outcomes focuses only on fractures and unclear if reference standard included a 2 week follow-up period

CT as index test

Table 10: Clinical evidence summary: CT

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Those meeting at least one NEXUS criterion, unclear if head injury, final diagnosis as reference standard, clinically significant injury as outcome												
Bailitz 2009 – high risk	1	Unclear (n=15 positive on reference standard)	Final diagnosis in medical record at discharge	Unclear	Clinically significant cervical spine injury – requiring operative procedure, halo application and/or rigid cervical collar	1.00 (0.78 to 1.00)	NR	Sensitivity				
								Very serious ^a	Very serious ^b	None	Serious ^c	VERY LOW
								Specificity NA				
Bailitz 2009 – moderate risk	1	Unclear (n=19 positive on reference standard)	Final diagnosis in medical record at discharge	Unclear	Clinically significant cervical spine injury – requiring operative procedure, halo application and/or rigid cervical collar	1.00 (0.82 to 1.00)	NR	Sensitivity				
								Very serious ^a	Very serious ^b	None	Serious ^c	VERY LOW
								Specificity NA				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Bailitz 2009 – low risk	1	Unclear (n=16 positive on reference standard)	Final diagnosis based on all prospectively collected clinical data and imaging results	Unclear	Clinically significant cervical spine injury – requiring operative procedure, halo application and/or rigid cervical collar	1.00 (0.79 to 1.00)	NR	Sensitivity					VERY LOW
								Very serious ^a	Very serious ^b	None	Serious ^c		
								Specificity					
					NA								
Mathen 2007 Risk stratification: those not meeting NEXUS low risk criteria	1	667	Final diagnosis based on all prospectively collected clinical data and imaging results	Unclear	Clinically significant cervical spine injury – requiring surgery or long-term stabilisation with a collar or halo	1.00 (0.87 to 1.00)	0.94 (0.92 to 0.96)	Sensitivity					VERY LOW
								Very serious ^a	Very serious ^b	None	Serious ^c		
								Specificity					
					Very serious ^a	Very serious ^b	None	None	VERY LOW				
Those failing NEXUS low risk criteria, unclear if head injury, final diagnosis as reference standard, clinically significant fractures as outcome													
Inaba 2016	1	10,276	Final diagnosis at discharge	Median length of stay was 2	Clinically significant cervical spine	0.98 (0.96 to 1.00)	0.91 (0.90 to 0.92)	Sensitivity					VERY LOW
								Very serious ^a	Very serious ^d	None	None		

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: patients failing low-risk NEXUS criteria			, including results of all imaging and operative findings	(IQR 1-6) days	fracture – requiring surgical stabilisation, Halo Orthotic placement or use of a Cervical-Thoracic Orthotic			Specificity				
								Very serious ^a	Very serious ^d	None	None	VERY LOW
Any with blunt injury and cervical spine assessed, unclear if head injury, reference standard unclear/final diagnosis, cervical spine injuries as outcome												
Duane 2016	1	9227	Later diagnosis of injury – poorly defined	Unclear	Fracture and/or ligamentous injury of cervical spine – no further details	1.00 (0.99 to 1.00)	1.00 (1.00 to 1.00)	Sensitivity				
Risk stratification: unclear, described as patients with criteria for trauma team alert								Very serious ^a	Very serious ^e	None	None	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^e	None	None	VERY LOW
	1	1199		Unclear			NR	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Griffen 2003			Unclear, possible all imaging/follow-up		Cervical spine injury - poorly defined	1.00 (0.97 to 1.00)		Very serious ^a	Very serious ^b	None	None	VERY LOW
Risk stratification: unclear								Specificity				
								NA				
Vanguri 2014	1	5676	Unclear, possibly including other imaging (such as MRI and flexion-extension radiographs depending on patient)	Unclear	Cervical spine injury – poorly defined	1.00 (0.99 to 1.00)	1.00 (1.00 to 1.00)	Sensitivity				
Risk stratification: unclear, those meeting criteria for trauma team activation								Very serious ^a	Very serious ^b	None	None	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^b	None	None	VERY LOW
Any with blunt injury and cervical spine assessment, unclear if head injury, reference standard unclear/final diagnosis, cervical spine fractures as outcome												
Nguyen 2005 – high risk	1	19	Diagnosis based on final reports including	Unclear	Cervical spine fractures – no	1.00 (0.78 to 1.00)	1.00 (0.82 to 1.00)	Sensitivity				
								Very serious ^a	Very serious ^f	None	Serious ^c	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
			all imaging		further details			Very serious ^a	Very serious ^f	None	None	VERY LOW	
Nguyen 2005 – low risk	1	78	Diagnosis based on final reports including all imaging	Unclear	Cervical spine fractures – no further details	Not estimable as there were no reference standard positive in this low-risk group	1.00 (0.99 to 1.00)	Sensitivity NA					
								Specificity					
								Very serious ^a	Very serious ^f	None	None	VERY LOW	
Ptak 2001	1	676	Final clinical diagnosis	Unclear	Cervical spine fracture – no further details	0.98 (0.91 to 1.00)	1.00 (0.99 to 1.00)	Sensitivity					
Risk stratification: unclear			, including operative and discharge notes (possibly incorporating CT results)					Very serious ^a	Very serious ^f	None	None	VERY LOW	
								Specificity					
								Very serious ^a	Very serious ^f	None	None	VERY LOW	
Any with suspected blunt cervical spine injury, >75% with head CT, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome													
Friesen 2013	1	206	MRI reported to be reference	Unclear	Any cervical spine injury –	0.83 (0.75 to 0.89)	Not estimable as no false positives possible when an index test forms	Sensitivity					
								Very serious ^a	None	None	None	LOW	
								Specificity					

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: 98% met at least one NEXUS criterion for imaging			standard in the paper, but data available to calculate using CT + MRI as reference standard		no further details		part of the reference standard	NA				
Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome												
Songur 2020	1	88	MRI reported to be reference	Unclear	Unstable cervical spine injury –	0.78 (0.67 to 0.86)	Not estimable as no false positives possible when an index test forms	Sensitivity				
								Very serious ^a	Serious ^g	None	Serious ^c	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear			standard in the paper, but data available to calculate using CT + MRI as reference standard		based on neurological status of the patient, degree of spinal canal stenosis, and the degree of instability . Denis' 1983 delineation was used in the definition of unstable injury		part of the reference standard	NA				
Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome												
Malhotra 2018	1	1080	MRI reported to be reference	Unclear	Any cervical spine injury	0.71 (0.67 to 0.75)	Not estimable as no false positives possible when an index test forms	Sensitivity				
								Very serious ^a	Serious ^g	None	Serious ^c	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear			standard in the paper, but data available to calculate using CT + MRI as reference standard		(including osseous and ligamentous injuries)		part of the reference standard	NA				
Novick 2018 Risk stratification: unclear	1	241	Reference standard not reported in the paper, but data available to calculate using CT + MRI as reference standard	Unclear	Cervical spine injuries (ligamentous or bony injuries)	0.87 (0.79 to 0.93)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity Very serious ^a Serious ^h None Serious ^c VERY LOW				
								Specificity NA				
Schoenfeld 2018	1	668	Reference standard not	Unclear	Cervical spine injury –	0.79 (0.73 to 0.84)	Not estimable as no false positives possible when an index test forms	Sensitivity Very serious ^a Serious ^g None None VERY LOW				
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear			reported in the paper, but data available to calculate using CT + MRI as reference standard		poorly defined		part of the reference standard	NA				

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled or it was clear convenience sampling was performed, it was unclear or unlikely that the index test and/or reference standard were interpreted without knowledge of the other, the time interval between index test and reference standard was unclear or likely inappropriate (>48 h) and it was unclear if the reference standard consisted of the same components for all patients or there was likely to be a difference in components between patients

^b Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard included a 2 week follow-up period

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^d Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and reference standard indirectness as outcome only includes fractures and does not involve a period of 2 weeks follow-up as specified in the protocol

^e Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard matches protocol as poorly defined

^f Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, outcomes focuses only on fractures and unclear if reference standard included a 2 week follow-up period

^g Downgraded by 1 increment as head injury not mentioned and unclear if all or most had head injury

^h Downgraded by 1 increment as head injury status only clear for 17%, unclear if others had suspected head injury/head imaging

MRI as index test

Table 11: Clinical evidence summary: MRI

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Any with suspected blunt cervical spine injury, >75% with head CT, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome												
Friesen 2013	1	108	MRI reported to be reference standard in the paper, but data available to calculate using CT + MRI as reference standard	Unclear	Any cervical spine injury – no further details	0.71 (0.62 to 0.78)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity Very serious ^a	None	None	Serious ^b	VERY LOW
Risk stratification: 98% met at least one NEXUS criterion for imaging								Specificity NA				
Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome												
	1	88		Unclear				Sensitivity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Songur 2020			MRI reported to be reference standard in the paper, but data available to calculate using CT + MRI as reference standard		Unstable cervical spine injury – based on neurological status of the patient, degree of spinal canal stenosis, and the degree of instability . Denis' 1983 delineation was used in the definition of unstable injury	1.00 (0.95 to 1.00)	Not estimable as no false positives possible when an index test forms part of the reference standard	Very serious ^a	Seriou ^s ^c	None	None	VERY LOW	
Risk stratification: unclear								Specificity NA					
Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome													
Malhotra 2018	1	1080	MRI reported to be reference	Unclear	Any cervical spine injury	0.83 (0.79 to 0.86)	Not estimable as no false positives possible when an index test forms	Sensitivity Very serious ^a					VERY LOW
								Seriou ^s ^c	None	None			
								Specificity					

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Risk stratification: unclear			standard in the paper, but data available to calculate using CT + MRI as reference standard		(including osseous and ligamentous injuries)		part of the reference standard	NA					
Novick 2018 Risk stratification: unclear	1	241	Reference standard not reported in the paper, but data available to calculate using CT + MRI as reference standard	Unclear	Cervical spine injuries (ligamentous or bony injuries)	0.77 (0.68 to 0.85)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity					VERY LOW
								Very serious ^a	Serious ^d	None	Serious ^b		
								Specificity NA					
Schoenfeld 2018	1	668	Reference standard not	Unclear	Cervical spine injury –	1.00 (0.99 to 1.00)	Not estimable as no false positives possible when an index test forms	Sensitivity					VERY LOW
								Very serious ^a	Serious ^c	None	None		
								Specificity					

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear			reported in the paper, but data available to calculate using CT + MRI as reference standard		poorly defined		part of the reference standard	NA				

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unclear or unlikely that the index test and/or reference standard were interpreted without knowledge of the other, and the time interval between index test and reference standard was unclear or likely inappropriate (>48 h)

^b Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^c Downgraded by 1 increment as head injury not mentioned and unclear if all or most had head injury

^d Downgraded by 1 increment as head injury status only clear for 17%, unclear if others had suspected head injury/head imaging

Adults – only including those admitted, not those subsequently discharged following index test

X-ray as index test

Table 12: Clinical evidence summary: X-ray

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Any admitted with blunt injury and cervical spine assessed, unclear if head injury, reference standard unclear/final diagnosis, cervical spine injuries as outcome													
Cohn 1991	1	60	Reference standard unclear, possibly final diagnosis based on any further imaging performed (including flexion/extension views, cervical CT scans or tomograms where indicated)	Unclear	Acute cervical spine injuries – poorly defined	0.57 (0.18 to 0.90)	NR	Sensitivity					VERY LOW
Risk stratification: unclear								Very serious ^a	Very serious ^b	None	Very serious ^c		
								Specificity					
NA													
Any admitted following trauma, unclear if head injury, CT as reference standard, cervical spine fractures as outcome													
Duane 2008	1	1004	CT of cervical spine	Unclear	Cervical spine fracture – no further details	0.19 (0.11 to 0.29)	0.99 (0.98 to 1.00)	Sensitivity					VERY LOW
Risk stratification								Very serious ^a	Very serious ^d	None	None		
								Specificity					

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
tion: unclear								Very serious ^a	Very serious ^d	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were (vary depending on the study): it was unclear whether or not a consecutive sample was enrolled, it was unclear whether the reference standard was interpreted without knowledge of the index test, the time interval between index test and reference standard was unclear and it was unclear if the reference standard consisted of the same components for all patients

^b Downgraded by 2 increments as head CT performed for 50% but unclear if remaining also had head injury as part of injury mechanism, and unclear if reference standard included a 2 week follow-up period

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^d Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and outcome limited to fractures rather than any cervical spine injury

CT as index test

Table 13: Clinical evidence summary: CT

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Any admitted following injury and cervical spine assessed, unclear if head injury, final diagnosis as reference standard, clinically significant cervical spine injuries as outcome													
Resnick 2014 Risk stratification: unclear	1	830	Final diagnosis at discharge (all imaging and operative findings)	Unclear	Clinically significant cervical spine injury – required either surgical intervention for stabilisation or halo placement, or mandatory use of a hard collar to protect an unstable ligamentous injury	1.00 (0.85 to 1.00)	1.00 (1.00 to 1.00)	Sensitivity					VERY LOW
								Very serious ^a	Very serious ^b	None	Serious ^c		
								Specificity					
								Very serious ^a	Very serious ^b	None	None	VERY LOW	

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were: it was unclear if the reference standard includes a period of at least 2 weeks follow-up, it was unclear if the reference standard was interpreted without knowledge of the index test and it was likely that the reference standard was slightly different between patients

^b Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard incorporates 2 week follow-up period specified in the protocol

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

Adults – only including those that are obtunded, unconscious and/or requiring intensive care unit admission

CT as index test

Table 14: Clinical evidence summary: CT

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
High risk trauma patients (pain, neurological symptoms or obtundation), unclear if head injury, final diagnosis as reference standard, any cervical spine injury as outcome												
Adams 2006	1	97	Final diagnosis based on MRI, CT and clinical decision-making of spinal consultants	Unclear	Cervical spine injury – poorly defined	0.94 (no raw data so CIs no calculable)	0.88 (no raw data so CIs no calculable)	Sensitivity				
Risk stratification: deemed high risk for axial trauma, unclear which stratification rule used								Very serious ^a	Very serious ^b	None	Serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^b	None	Serious ^d	VERY LOW
High risk severely injured patients, unclear if head injury, final diagnosis as reference standard, cervical spine abnormality as outcome												
	1	102					NR	Sensitivity				

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Widder 2004			Final diagnosis at discharge considering any readmissions	Unclear, suggests follow-up post-discharge as readmissions mentioned	Cervical spine abnormality – poorly defined	1.00 (0.81 to 1.00)		Serious ^a	Serious ^e	None	Serious ^c	VERY LOW
Risk stratification: high-risk severely injured patients, unclear which stratification rule used								Specificity NA				
High risk blunt trauma and admission to intensive care unit, unclear if head injury, final diagnosis as reference standard, unstable cervical spine injury as outcome												
Berne 1999	1	58	Final diagnosis based on all	Unclear	Unstable cervical spine injury – in consultation	1.00 (0.63 to 1.00)	1.00 (0.93 to 1.00)	Sensitivity				
Risk stratification								Very serious ^a	Very serious ^f	None	Very serious ^c	VERY LOW
								Specificity				

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
tion: described as high-risk blunt trauma, unclear which stratification rule used			imaging/studies		on with neurosurgical-orthopaedic spine service based on published guidelines			Very serious ^a	Very serious ^f	None	None	VERY LOW	
Unconscious intubated trauma patients, unclear if head injury, final diagnosis as reference standard, unstable cervical spine injury as outcome													
Brohi 2005	1	381	Final diagnosis, including all imaging performed (MRI in some) and follow-up through hospital stay	Unclear, through hospital stay	Unstable cervical spine injury – using White and Punjabi and three-column model of Denis	1.00 (0.88 to 1.00)	0.99 (0.97 to 1.00)	Sensitivity					
Risk stratification: not reported, but all were unconscious, intubated patients								Very serious ^a	Very serious ^g	None	Serious ^c	VERY LOW	
								Specificity					
								Very serious ^a	Very serious ^g	None	None	VERY LOW	
Altered sensorium admitted following injury and cervical spine assessed, unclear if head injury, final diagnosis as reference standard, clinically significant cervical spine injuries as outcome													
Raza 2013	1	53	Final diagnosis of injury	Unclear duration,	Clinically significant cervical	1.00 (no raw data so CIs no calculable)	NR	Sensitivity					
								Very serious ^a	Serious ^h	None	Very serious ^c	VERY LOW	

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: high-risk severely injured patients, unclear which stratification rule used			at hospital discharge, follow-up appointments or any readmissions	includes follow-up post-discharge as readmissions mentioned	spine injury – poorly defined			Specificity NA				
Obtunded with intracranial haemorrhage diagnosis following non high-impact trauma, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome												
Tan 2014	1	83	MRI reported to be reference standard in the paper, but data available to calculate using CT + MRI as reference standard	Unclear	Unstable cervical spine injury – poorly defined	1.00 (no raw data so CIs no calculable)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity Very serious ^a Serious ^h None Serious ^c VERY LOW				
Risk stratification: unclear, all obtunded patients admitted to ICU with intracranial haemorrhage								Specificity NA				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Obtunded patients, possibly all had brain assessment, CT + MRI as reference standard (only sensitivity possible), any cervical spine injuries as outcome													
Lau 2018 Risk stratification: unclear, all unconscious requiring mechanical ventilation	1	63	MRI reported to be reference standard in the paper, but data available to calculate using CT + MRI as reference standard	Unclear	Cervical spine injuries – poorly defined but appears to include bony and ligamentous injuries	0.872 (no raw data so CIs no calculable)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity					VERY LOW
								Very serious ^a	Serious ^h	None	Very serious ^c		
								Specificity					
					NA								
Obtunded patients (mostly adults), unclear if head injury, CT + MRI as reference standard (only sensitivity possible), clinically significant cervical spine injury as outcome													
Fisher 2013	1	277	Diagnosis of clinically significant	Unclear	Clinically significant cervical spine	0.83 (no raw data so CIs no calculable)	Not estimable as no false positives possible when an index test forms	Sensitivity					VERY LOW
								Very serious ^a	Serious ^h	None	Serious ^c		
								Specificity					

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear, all obtunded patients			Gold standard: cervical spine injury by any modality (CT or MRI)		injury – ligamentous injury in two adjacent spinal columns, subluxations, cord injury, nerve root injury, disc herniations, and fractures except those specified in NEXUS		part of the reference standard	NA				
Unconscious adults, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome												
Parmar 2018	1	27	MRI reported to be reference	Unclear	Cervical spine injuries – poorly	0.74 (0.54 to 0.89)	Not estimable as no false positives possible when an index test forms	Sensitivity				
								Very serious ^a	Serious ⁱ	None	Serious ^c	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear, all unconscious requiring mechanical ventilation			standard in the paper, but data available to calculate using CT + MRI as reference standard		defined but appears to include bony and ligamentous injuries		part of the reference standard	NA				

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unclear or unlikely that the index test and/or reference standard were interpreted without knowledge of the other, the time interval between index test and reference standard was unclear or likely inappropriate (>48 h), and it was unclear whether or likely that the components of the reference standard differed between patients

^b Downgraded by 2 increments as all included were high-risk representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and it is unclear if the reference standard included a 2-week follow-up period and reference standard possibly places focus on MRI results

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use. Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^d Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^e Downgraded by 1 increment as all were within more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

^f Downgraded by 2 increments as all were high-risk representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and unclear if reference standard included a 2 week follow-up period

^g Downgraded by 2 increments as all were unconscious representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and unclear if reference standard included a 2 week follow-up period

^h Downgraded by 1 increment as all were obtunded representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

ⁱ Downgraded by 1 increment as all were unconscious representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

MRI as index test

Table 15: Clinical evidence summary: MRI

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Obtunded with intracranial haemorrhage diagnosis following non high-impact trauma, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome												
Tan 2014	1	83	MRI reported to be reference	Unclear	Unstable cervical spine injury –	1.00 (no raw data so CIs no calculable)	Not estimable as no false positives possible when an index test forms	Sensitivity Very serious ^a	Serious ^b	None	Serious ^c	VERY LOW
								Specificity				

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Risk stratification: unclear, all obtunded patients admitted to ICU with intracranial haemorrhage			standard in the paper, but data available to calculate using CT + MRI as reference standard		poorly defined		part of the reference standard	NA					
Obtunded patients, possibly all had brain assessment, CT + MRI as reference standard (only sensitivity possible), any cervical spine injuries as outcome													
Lau 2018	1	63	MRI reported to be reference standard in the paper, but data available to calculate using CT + MRI as reference standard	Unclear	Cervical spine injuries – poorly defined but appears to include bony and ligamentous injuries	1.00 (no raw data so CIs no calculable)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity					
Risk stratification: unclear, all unconscious requiring mechanical ventilation								Very serious ^a	Serious ^b	None	Very serious ^c	VERY LOW	
								Specificity					
								NA					

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Obtunded patients (mostly adults), unclear if head injury, CT + MRI as reference standard (only sensitivity possible), clinically significant cervical spine injury as outcome													
Fisher 2013	1	277	Diagnoses of clinically significant cervical spine injury by any modality (CT or MRI)	Unclear	Clinically significant cervical spine injury – ligamentous injury in two adjacent spinal columns, subluxations, cord injury, nerve root injury, disc herniations, and fractures except those specified in NEXUS	0.89 (no raw data so CIs not calculable)	Not estimable as no false positives possible when an index test forms part of the reference standard	Sensitivity					VERY LOW
Risk stratification: unclear, all obtunded patients								Very serious ^a	Serious ^b	None	Serious ^c		
								Specificity					
								NA					
Unconscious adults, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome													
	1	27		Unclear				Sensitivity					

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Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Parmar 2018			MRI reported to be reference standard in the paper, but data available to calculate using CT + MRI as reference standard		Cervical spine injuries – poorly defined but appears to include bony and ligamentous injuries	0.96 (0.81 to 1.00)	Not estimable as no false positives possible when an index test forms part of the reference standard	Very serious ^a	Serious ^d	None	Serious ^c	VERY LOW
Risk stratification: unclear, all unconscious requiring mechanical ventilation								Specificity				

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unlikely that the index test and reference standard were interpreted without knowledge of the other, and the time interval between index test and reference standard was unclear or likely inappropriate (>48 h)

^b Downgraded by 1 increment as all were obtunded representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use. Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^d Downgraded by 1 increment as all were unconscious representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

Adults – other very specific populations

X-ray as index test

Table 16: Clinical evidence summary: X-ray

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Those with diffuse idiopathic skeletal hyperostosis with low energy trauma, unclear if head injury, whole spine CT as reference standard, acute fracture of cervical spine as outcome													
Dan Lantsman 2020	1	129	Whole spine CT scan	Possibly at least 1 month but unclear	Acute cervical spine fracture – those not present in previous imaging of patient and involving cortical disruption or impaction of trabeculae and paravertebral soft tissue infiltration	0.00 (no raw data so CIs no calculable)	1.00 (no raw data so CIs no calculable)	Sensitivity					VERY LOW
								Serious ^a	Very serious ^b	None	Serious ^c		
Risk stratification: unclear								Specificity					VERY LOW
								Serious ^a	Very serious ^b	None	Serious ^d		

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Those with blunt trauma with CT and flexion-extension radiographs for continued cervical pain (fractures already excluded), unclear if head injury, all available evidence as reference standard, ligamentous cervical spine injury as outcome												
Goodnight 2008 (flexion-extension X-rays)	1	379	All available evidence, including MRI in some patients	Unclear	Ligamentous cervical spine injury – poorly defined	1.00 (0.54 to 1.00)	0.97 (0.95 to 0.99)	Sensitivity				
								Very serious ^a	Very serious ^e	None	Very serious ^c	VERY LOW
Risk stratification: unclear								Specificity				
								Very serious ^a	Very serious ^e	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were (vary depending on the study): it was unclear whether or not a consecutive sample was enrolled, it was unclear whether the reference standard was interpreted without knowledge of the index test, the time interval between index test and reference standard was unclear, not all patients were analysed due to missing radiographs or poor quality radiographs, and it was unlikely that the reference standard consisted of the same components for all patients

^b Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, it was a very specific population of those with DISH, a condition making injuries more likely following lower impact trauma, and injury reported was specifically fracture not any type of injury

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use. Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^d Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^e Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, population where those with confirmed fractures were excluded meaning may differ from population presenting without any prior imaging, outcome limited to ligamentous injuries and unclear if reference standard included a 2 week follow-up period

CT as index test

Table 17: Clinical evidence summary: CT

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Intoxicated adults with blunt trauma, unclear if head injury, final/discharge diagnosis as reference standard, unstable cervical spine injury as outcome													
Bush 2016	1	631	Status at discharge /follow-up, including MRI findings, operative findings and clinical status at discharge	Unclear	Unstable cervical spine injury – any unstable or potentially unstable injury that required surgical stabilisation or prolonged immobilisation	0.93 (0.66 to 1.00)	1.00 (0.99 to 1.00)	Sensitivity					VERY LOW
Risk stratification: unclear, but all intoxicated adults								Very serious ^a	Very serious ^b	None	Very serious ^c		
								Specificity					VERY LOW
								Very serious ^a	Very serious ^b	None	None		
Those with blunt trauma with CT and flexion-extension radiographs for continued cervical pain, unclear if head injury, all available evidence as reference standard, ligamentous cervical spine injury as outcome													

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Goodnight 2008 (flexion-extension X-rays) Risk stratification: unclear	1	379	All available evidence, including MRI in some patients	Unclear	Ligamentous cervical spine injury – poorly defined	1.00 (0.54 to 1.00)	0.97 (0.94 to 0.98)	Sensitivity				
								Very serious ^a	Very serious ^d	None	Very serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^d	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were (vary depending on the study): it was unclear whether or not a consecutive sample was enrolled, reasons for exclusion were not reported, the follow-up period for assessing the reference standard was unclear, it was unclear whether the reference standard was interpreted without knowledge of the index test, the time interval between index test and reference standard was unclear, and it was unlikely that the reference standard consisted of the same components for all patients

^b Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, also limited to very specific population of those that were intoxicated and unclear time-point for reference standard and whether it matches protocol

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^d Downgraded by 2 increments as head injury not mentioned and unclear if all or most had head injury, population where those with confirmed fractures were excluded meaning may differ from population presenting without any prior imaging, outcome limited to ligamentous injuries and unclear if reference standard included a 2 week follow-up period

Children – all having index test and not limited to those that were admitted

X-ray as index test

Table 18: Clinical evidence summary: X-ray

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Children with possible neck injury, 40% had head CT, reference standard unclear/follow-up/other imaging, cervical spine injury as outcome												
Somppi 2018 Risk stratification: unclear	1	495	Unclear, possibly all imaging and follow-up	Follow-up of records for up to 1 month after index ED visit	Cervical spine injury (ligamentous and osseous injuries)	0.83 (0.36 to 0.99)	0.97 (0.96 to 0.99)	Sensitivity				
								Very serious ^a	Very serious ^b	None	Very serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^b	None	None	VERY LOW
Children with cervical spine imaging, unclear if head injury, reference standard as CT, cervical spine injury as outcome												
Rana 2009 Risk stratification: unclear	1	54	CT of cervical spine	Unclear	Cervical spine injury – poorly defined	0.615 (no raw data so CIs no calculable)	0.016 (no raw data so CIs no calculable)	Sensitivity				
								Very serious ^a	Serious ^d	None	Very serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Serious ^d	None	Very serious ^e	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were (vary depending on the study): it was unclear whether or not a consecutive sample was enrolled, it was unclear whether the index test and/or reference standard was interpreted without knowledge of the other, the reference standard used for each index test was unclear, the time interval

between index test and reference standard was unclear, and it was unclear whether the reference standard consisted of the same components for all patients

^b Downgraded by 2 increments as unclear if all or the majority also sustained a head injury (40% said to have had head CT) and reference standard poorly defined so unclear if matches protocol

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use. Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^d Downgraded by 1 increment as unclear if all or the majority also sustained a head injury

^e Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

CT as index test

Table 19: Clinical evidence summary: CT

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Children with possible neck injury, 40% had head CT, reference standard unclear/follow-up/other imaging, cervical spine injury as outcome												
Somppi 2018	1	130	Unclear, possibly all imaging and follow-up	Follow-up of records for up to 1 month after index ED visit	Cervical spine injury (ligamentous and osseous injuries)	1.00 (0.52 to 1.00)	1.00 (0.96 to 1.00)	Sensitivity				
								Very serious ^a	Very serious ^b	None	Very serious ^c	VERY LOW
Risk stratification: unclear								Specificity				
								Very serious ^a	Very serious ^b	None	None	VERY LOW
Children with cervical spine imaging, unclear if head injury, reference standard as other imaging findings (unclear), cervical spine injury as outcome												
	1	54		Unclear				Sensitivity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Rana 2009			Clinical outcome, including subsequent imaging where performed		Cervical spine injury – poorly defined	1.00 (no raw data so CIs not calculable)	0.976 (no raw data so CIs not calculable)	Very serious ^a	Very serious ^d	None	Very serious ^c	VERY LOW	
Risk stratification: unclear								Specificity				Very serious ^a	Very serious ^d
Children following trauma, unclear if head injury, reference standard as final diagnosis/unclear, unstable cervical spine injuries as outcome													
Derderian 2019	1	221	Unclear, confirmed clinical instability	Unclear	Unstable cervical spine injury –	1.00 (0.89 to 1.00)	0.85 (0.79 to 0.90)	Sensitivity					VERY LOW
								Very serious ^a	Serious ^f	None	Serious ^c		
								Specificity					

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Risk stratification: unclear			– records of those undergoing intervention		surgical intervention (spinal fusion or halo placement) indicated clinically unstable while radiologically unstable were those with disruption of two or more spinal columns (defined by Denis)			Very serious ^a	Serious ^f	None	None	VERY LOW	
Children following trauma, unclear if head injury, reference standard as MRI, any soft tissue cervical spine injury as outcome													
Henry 2013-2	1	84	MRI of cervical spine	Unclear	Soft tissue injury of cervical spine –	0.23 (0.05 to 0.54)	1.00 (0.95 to 1.00)	Sensitivity					VERY LOW
Risk stratification								Very serious ^a	Very serious ^g	None	None		
								Specificity					

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
tion: unclear					soft tissue oedema, ligamentous injury, muscular injury and spinal cord injury			Very serious ^a	Very serious ^g	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unclear whether or unlikely that the index test and/or reference standard was interpreted without knowledge of the other, the time interval between index test and reference standard was unclear, and it was unclear whether the reference standard consisted of the same components for all patients

^b Downgraded by 2 increments as unclear if all or the majority also sustained a head injury (40% said to have had head CT) and reference standard poorly defined so unclear if matches protocol

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use. Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^d Downgraded by 2 increments as unclear if all or the majority also sustained a head injury, and unclear if follow-up of at least 2 weeks as part of the reference standard

^e Where confidence intervals could not be calculated due to lack of raw data reporting, studies were downgraded by 1 increment if the sample size was ≥ 70 and < 350 and by 2 increments if the sample size was < 70 .

^f Downgraded by 1 increment as unclear if all or the majority also sustained a head injury

^g Downgraded by 2 increments as unclear if all or the majority also sustained a head injury and outcome limited to ligamentous injury not any cervical spine injury

MRI as index test

Table 20: Clinical evidence summary: MRI

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Children with possible neck injury, 40% had head CT, reference standard unclear/follow-up/other imaging, cervical spine injury as outcome												
Somppi 2018	1	21	Unclear, possibly all imaging and follow-up	Follow-up of records for up to 1 month after index ED visit	Cervical spine injury (ligamentous and osseous injuries)	1.00 (0.51 to 1.00)	1.00 (0.75 to 1.00)	Sensitivity				
								Very serious ^a	Very serious ^b	None	Very serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Very serious ^b	None	None	VERY LOW
Children following trauma, unclear if head injury, reference standard as final diagnosis/unclear, unstable cervical spine injuries as outcome												
Derderian 2019	1	221	Unclear, confirmed clinical instability	Unclear	Unstable cervical spine injury –	1.00 (0.89 to 1.00)	0.45 (0.37 to 0.52)	Sensitivity				
								Very serious ^a	Serious ^d	None	Serious ^c	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Risk stratification: unclear			– records of those undergoing intervention		surgical intervention (spinal fusion or halo placement) indicated clinically unstable while radiologically unstable were those with disruption of two or more spinal columns (defined by Denis)			Very serious ^a	Serious ^d	None	Serious ^e	VERY LOW	
Henry 2013-1	1	73	Injury requiring surgical intervention	Follow-up mean	Cervical spine instability –	1.00 (0.03 to 1.00)	0.97 (0.90 to 1.00)	Sensitivity					
								Very serious ^a	Serious ^d	None	Very serious ^c	VERY LOW	
								Specificity					

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Risk stratification: unclear, those that could not be cleared clinically			on or presenting with clinical or radiographic evidence of instability on follow-up	10.0 months	requiring surgical stabilisation			Very serious ^a	Serious ^d	None	None	VERY LOW	
Children following trauma, unclear if head injury, reference standard as CT, any osseous cervical spine injury as outcome													
Henry 2013-2	1	84	CT of cervical spine	Unclear	Osseous injury of cervical spine – fractures, locked facets, subluxations and dislocations	1.00 (0.54 to 1.00)	0.97 (0.91 to 1.00)	Sensitivity					
Risk stratification: unclear								Very serious ^a	Very serious ^f	None	Very serious ^c	VERY LOW	
								Specificity					
								Very serious ^a	Very serious ^f	None	None	VERY LOW	

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unclear whether or unlikely that the index test and/or reference standard was interpreted without knowledge of the other, the time interval between index test and reference standard was unclear, and it was unclear whether the reference standard consisted of the same components/same follow-up for all patients

^b Downgraded by 2 increments as unclear if all or the majority also sustained a head injury (40% said to have had head CT) and reference standard poorly defined so unclear if matches protocol

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^d Downgraded by 1 increment as unclear if all or the majority also sustained a head injury

^e Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.7 and 0.4, respectively, which were the thresholds used for specificity to determine if an imaging test should be recommended or was of no clinical use

^f Downgraded by 2 increments as unclear if all or the majority also sustained a head injury and outcome limited to fractures not any cervical spine injury

Children – only including those that are obtunded, unconscious and/or requiring intensive care unit admission

X-ray as index test

Table 21: Clinical evidence summary: X-ray

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Children with severe injuries admitted to intensive care unit, unclear if head injury, reference standard as clinical outcome/diagnosis at time of discharge/latest follow-up, cervical spine instability requiring surgery as outcome												
Brockmeyer 2012	1	24	Clinical outcome/diagnosis of early	Possibly >2 weeks as	Early cervical spine instability	1.00 (0.03 to 1.00)	0.96 (0.78 to 1.00)	Sensitivity Very serious ^a	Serious ^b	None	Very serious ^c	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear, all comatose with severe traumatic injuries			instability – undergoing surgical correction	mention plain radiographs at follow-up of 3-4 months post-injury	– surgical correction			Very serious ^a	Serious ^b	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were: it was unclear if index tests and reference standard were interpreted without knowledge of the other, time interval between index tests and reference standard was unclear, and it was unclear if the reference standard consisted of the same components for all patients

^b Downgraded by 1 increment as all were within a severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

CT as index test

Table 22: Clinical evidence summary: CT

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Children with cervical spine assessment and confirmed severe traumatic brain injury, reference standard as CT + MRI possibly other imaging, unstable cervical spine injury as outcome												

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Qualls 2015 Risk stratification: unclear, all with severe traumatic brain injury	1	63	Final diagnosis based on all imaging reports (CT, MRI and possibly other imaging)	Unclear	Unstable cervical spine injury – injuries resulting in neurological deficit localised to cervical spine cord, cooperative stabilisation, halo placement or cervical immobilisation of 3 months or greater	1.00 (0.48 to 1.00)	0.84 (0.73 to 0.93)	Sensitivity				
								Very serious ^a	Serious ^b	None	Very serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Serious ^b	None	None	VERY LOW
Children with severe injuries/unconscious, unclear if head injury, reference standard as final diagnosis/all information, injuries requiring stabilisation/surgical correction as outcome												
Al-Sarheed 2020	1	65	Radiology/clinical examination, including	Unclear	Cervical spine injury requiring	0.85 (0.68 to 0.95)	1.00 (0.89 to 1.00)	Sensitivity				
								Very serious ^a	Very serious ^d	None	Very serious ^c	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear, all were unconscious and intubated			MRI for some where performed		stabilisation			Very serious ^a	Very serious ^d	None	None	VERY LOW
Brockmeyer 2012 Risk stratification: unclear, all comatose with severe traumatic injuries	1	24	Clinical outcome/diagnosis of early instability – undergoing surgical correction	Possibly >2 weeks as mention plain radiographs at follow-up of 3-4 months post-injury	Early cervical spine instability – surgical correction	1.00 (0.03 to 1.00)	1.00 (0.85 to 1.00)	Sensitivity				
								Very serious ^a	Serious ^e	None	Very serious ^c	VERY LOW
								Specificity				
								Very serious ^a	Serious ^e	None	None	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Common issues contributing to risk of bias were: it was unclear whether or not a consecutive sample was enrolled, it was unclear whether or unlikely that the index test and/or reference standard was interpreted without knowledge of the other, the time interval between index test and reference standard was unclear or not appropriate (>48 h), and it was unclear whether or clear that the reference standard did not consist of the same components for all patients

^b Downgraded by 1 increment as all were within a severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^d Downgraded by 2 increments as all were unconscious representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and unclear if the reference standard matches protocol as definition provided is limited to 'radiology/clinical examination'

^e Downgraded by 1 increment all were within a severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

MRI as index test

Table 23: Clinical evidence summary: MRI

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE	
Children with cervical spine assessment and confirmed severe traumatic brain injury, reference standard as CT + MRI possibly other imaging, unstable cervical spine injury as outcome													
Qualls 2015	1	63	Final diagnosis based on all	Unclear	Unstable cervical spine injury –	0.80 (0.28 to 0.99)	0.91 (0.69 to 0.90)	Sensitivity					VERY LOW
								Very serious ^a	Serious ^b	None	Very serious ^c		
								Specificity					

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear, all with severe traumatic brain injury			imaging reports (CT, MRI and possibly other imaging)		injuries resulting in neurological deficit localised to cervical spine cord, cooperative stabilisation, halo placement or cervical immobilisation of 3 months or greater			Very serious ^a	Serious ^b	None	Serious ^d	VERY LOW
Children with severe injuries admitted to intensive care unit, unclear if head injury, reference standard as clinical outcome/diagnosis at time of discharge/latest follow-up, cervical spine instability requiring surgery as outcome												
Brockmeyer 2012	1	24	Clinical outcome/diagnosis of early	Possibly >2 weeks as	Early cervical spine instability	1.00 (0.03 to 1.00)	0.74 (0.52 to 0.90)	Sensitivity Very serious ^a	Serious ^e	None	Very serious ^c	VERY LOW
								Specificity				

FINAL
Imaging of the cervical spine

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Risk stratification: unclear, all comatose with severe traumatic injuries			instability – undergoing surgical correction	mention plain radiographs at follow-up of 3-4 months post-injury	– surgical correction			Very serious ^a	Serious ^e	None	Serious ^d	VERY LOW

^a Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Issues contributing to risk of bias were (varied depending on study): it was unclear whether or not a consecutive sample was enrolled, it was unclear whether or unlikely that the index test and/or reference standard was interpreted without knowledge of the other, the time interval between index test and reference standard was unclear or not appropriate (>48 h), and it was unclear whether or clear that the reference standard did not consist of the same components for all patients

^b Downgraded by 1 increment as all were within a severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

^c Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if an imaging test should be recommended or was of no clinical use

^d Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.7 and 0.4, respectively, which were the thresholds used for specificity to determine if an imaging test should be recommended or was of no clinical use

^e Downgraded by 1 increment as all were within a severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury

1.1.7 Economic evidence

1.1.7.1 Included studies

No published health economic studies were included. However, two models were identified from previous NICE guidelines:

- NICE Head injury guideline (CG176) 2014 - <https://www.nice.org.uk/guidance/cg176/evidence/appendices-pdf-191719838> (Appendix M)
- NICE Spinal injury guideline (NG41) 2016 - <https://www.nice.org.uk/guidance/ng41/evidence/appendices-jp-pdf-2358425775> (Appendix L)

These economic evaluations are described in section 1.1.8 Summary of included economic evidence.

1.1.7.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix F.

1.1.8 Summary of included economic evidence

A description of two relevant guideline models can be found in Table 24 with an assessment of their applicability and quality. Table 25 shows a description of the CG176 model strategies. It indicates the implausible assumption in the base case where far more people have X-ray than CT in the CT strategy, Strategy 5. The sensitivity analysis in the lower panel seem more plausible and will be the focus of this review.

Table 24: Comparison of previous guideline model characteristics

	NICE Head injury guideline (CG176) 2014	NICE spinal injury guideline (NG41) 2016
Comparators	7 strategies Canadian C-Spine rule vs NEXUS c-spine rule vs image all vs no CT vs X-ray (then MRI if positive or indeterminate)	18 strategies Canadian C-Spine rule vs NEXUS c-spine rule vs image all CT vs X-ray vs MRI Further imaging after a positive scan
Population	Adults with suspected cervical spine injury <u>and head injury</u>	Adults with suspected (cervical) spinal column injury (bony or ligamentous) and <u>no other injuries</u>
Perspective	NHS & personal social services	NHS & personal social services
Study design	Decision tree	Decision tree
Main outcome	False negatives averted	Quality-adjusted life-years (QALYs)
Applicability assessment	Partially applicable Due to absence of quality-adjusted life-years (or any measure of health outcome).	Partially applicable Due to population not being exclusively people with head injury.
Time horizon	Hospital episode	Lifetime
Treatment effects	95% of missed spinal injuries deteriorate with a cost of £7,214	0.5% of missed column injuries convert to a cord injury
Cost components	<ul style="list-style-type: none"> Imaging costs (x-ray, CT and MRI) Observation (depending on test results) Treatment Litigation cost (in a secondary analysis) 	<ul style="list-style-type: none"> Imaging costs (x-ray, CT and MRI) Treatment of column injury (depending on whether true positive, false positive or false negative) Spinal cord injury Litigation cost Cancer treatment cost from radiation

	NICE Head injury guideline (CG176) 2014	NICE spinal injury guideline (NG41) 2016
Limitations	<ul style="list-style-type: none"> • Most probabilities in model based on expert opinion <ul style="list-style-type: none"> ○ Indeterminate results ○ Accuracy of tests after an indeterminate test or 2nd-line test • Specificity of prediction rule differed a lot for CT and X-ray in the base case analysis. How they were applied in the model was not clearly described. Furthermore, the strategy labelled “CT according to Canadian C-Spine rule” actually had fewer CT scans in the base case analysis than the strategy labelled “X-ray according to Canadian C-Spine rule for CT”. This is due to the specificity of CT being misapplied in the model and due to the assumption in both strategies that 50% of false negatives get the other imaging modality. However, there was a sensitivity analysis with far more plausible assumptions for the Canadian C-spine rule strategies – see Table 25. 	<ul style="list-style-type: none"> • Does not explicitly model the pathway for indeterminate results • Assumes accuracy of 2nd-line test is independent of 1st test result • Prevalence and evidence for treatment effects based on expert opinion
Quality assessment	Potentially serious limitations	Potentially serious limitations

Table 25: Specification of strategies in head injury guideline model (CG176)

a) Base case analysis

Probability of having a given initial image strategy	Initial clinical decision (for those without injury)			Initial clinical decision (for those with injury)		
	No imaging	CT first	X ray first	No imaging	CT first	X ray first
7						
Strategy 1: No imaging	100%			100%		
Strategy 2: CT all		100%			100%	
Strategy 3: x ray all			100%			100%
Strategy 4: Canadian C spine for Xray	29%	29%	43%	0%	0%	100%
Strategy 5: Canadian C Spine for CT	49.7%	0.6%	49.7%	0%	100%	0%
Strategy 6: NEXUS for Xray	32%	32%	37%	4.65%	4.65%	90.70%
Strategy 7: NEXUS for CT	38%	24%	38%	5%	90%	5%

b) Sensitivity analysis: 'Committee estimates for initial imaging decisions'

Probability of having a given initial image strategy	Initial clinical decision (for those without injury)			Initial clinical decision (for those with injury)		
	No imaging	CT first	X ray first	No imaging	CT first	X ray first
7						
Strategy 1: No imaging	100%			100%		
Strategy 2: CT all		100%			100%	
Strategy 3: x ray all			100%			100%
Strategy 4: Canadian C spine for Xray	54%	3%	43%	0%	0%	100%
Strategy 5: Canadian C Spine for CT	54%	46%	0%	0%	100%	0%
Strategy 6: NEXUS for Xray	60%	3%	37%	4.65%	4.65%	90.70%
Strategy 7: NEXUS for CT	22%	40%	38%	5%	90%	5%

Table 25 shows for the CG176 model, the proportion of people having each test for those who do have an underlying spine injury and those that do not. This is shown for every comparator in the base case analysis (top panel) and for a key sensitivity analysis (bottom panel) – For details see

H.1.3.3 and H.1.4 of Appendix H below. The prevalence of injury was only 0.5% therefore the left-hand side of the table covers most patients. In the base case analysis (top panel) CT strategy 5, 49.7% of these patients had an X-ray and only 0.6% had a CT scan. Paradoxically in X-ray strategy 4, 29% had a CT, which was more than in the CT strategy. The current committee concluded that this was illogical and therefore only considered the results of the model based on the sensitivity analysis.

Table 26 compares the estimates of accuracy used in each model with those found in the current guideline review.

Table 26: Diagnostic accuracy of imaging used in previous guideline models

	Head injury guideline model (CG176)	Spinal injury guideline model (NG41)	2021 guideline review – see 1.1.6. (depending on reference standard)
X-ray Sensitivity	56.8%	70%	32%-65%
X-ray Specificity	99.7%	84%	95%-99%
CT sensitivity	83.0%	98%	93%-100%
CT specificity	99.9%	100%	91%-100%

Error! Not a valid bookmark self-reference. and Table 28 show the results of each model. Both models found the use of CT with the Canadian C-Spine CT rule to be the most cost-effective strategy.

For the 2014 head injury guideline model, we can say little about the sensitivity of results, because the guideline’s sensitivity analyses were based on variations from its flawed base case analysis. For the spinal injury guideline model, there was a lot of uncertainty around model parameters but it was concluded that the results were robust to plausible changes

- in the accuracy estimates,
- in the discount rate,
- when litigation costs were included,
- when the QALY loss associated with false negatives was increased,
- when the time horizon was extended,
- when the risk and consequences of radiation exposure were included.

The spinal injury guideline concluded that at the assumed prevalence rates and accuracy data, CT scans in combination with a decision rule are most likely to be cost effective. Therefore, CT scanning only those with a positive X-ray at the assumed prevalence and accuracy rates results in many missed injuries.

Table 27: Sensitivity analysis^a results from NICE head injury model (CG176): ‘Committee estimates for initial imaging decisions’

Strategy	Mean cost	False negatives	Cost per false negative avoided (vs no imaging)	Mean cost including litigation cost ^b	Rank ^c
No imaging	£1 ^d	0.500%		£1,001	6
CT all	£329	0.140%	£90,974	£612	2
X-ray all	£558	0.280%	£253,076	£1,116	7
Canadian C-spine rule for Xray	£335	0.280%	£151,890	£893	5
Canadian C-Spine rule for CT	£295	0.140%	£81,478	£578	1
NEXUS C-Spine rule for Xray	£311	0.280%	£140,780	£877	4
NEXUS C-Spine rule for CT	£301	0.170%	£90,866	£633	3

(a) The base case analysis results are fatally flawed. A plausible sensitivity analysis is reported here instead.

(b) Litigation cost was assumed to be £200,000 for each false negative test result.

(c) Rank of mean cost including litigation cost – 1=lowest cost, 7=highest cost.

(d) In the no imaging arm, almost all patients were discharged and there were no treatment costs. There were observation costs for a very small proportion of patients.

Table 28: Base case results from NICE spinal injury model (NG41)

Strategy	Mean cost	Mean Quality-adjusted life-years	Net Health Benefit (£20K per QALY)*	Rank
1. X-ray	£158	20.85252	20.8446	14
2. CT	£121	20.85275	20.8467	7
3. MRI	£191	20.85270	20.8431	18
4. X-ray + CT	£127	20.85251	20.8461	12
5. CT + MRI	£129	20.85268	20.8462	11
6. MRI + CT	£187	20.85268	20.8433	17
7. Canadian C-spine rule + X-ray	£111	20.85252	20.8470	5
8. Canadian C-spine rule + CT	£81	20.85275	20.8487	1
9. Canadian C-spine rule + MRI	£122	20.85270	20.8466	9
10. NEXUS C-spine rule + X-ray	£146	20.85252	20.8452	13
11. NEXUS C-spine rule + CT	£111	20.85274	20.8472	4
12. NEXUS C-spine rule + MRI	£173	20.85269	20.8440	16
13. Canadian C-spine rule + X-ray + CT	£95	20.85251	20.8478	3
14. Canadian C-spine rule + CT + MRI	£89	20.85267	20.8482	2
15. Canadian C-spine rule + MRI + CT	£121	20.85267	20.8466	8
16. NEXUS C-spine rule + X-ray + CT	£119	20.85251	20.8466	10
17. NEXUS C-spine rule + CT + MRI	£119	20.85267	20.8467	6
18. NEXUS C-spine rule + MRI + CT	£170	20.85267	20.8442	15

1.1.9 Economic model

Original modelling was not conducted for this guideline. The model from CG176 was summarised in 1.1.8 above and the full report can be found in Appendix H.

1.1.10 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Code	Description	Unit cost
RD01A	Magnetic Resonance Imaging Scan of One Area, without Contrast, 19 years and over	£146.75
RD01B	Magnetic Resonance Imaging Scan of One Area, without Contrast, between 6 and 18 years	£215.63
RD01C	Magnetic Resonance Imaging Scan of One Area, without Contrast, 5 years and under	£140.83
RD20A	Computerised Tomography Scan of One Area, without Contrast, 19 years and over	£88.06
RD20B	Computerised Tomography Scan of One Area, without Contrast, between 6 and 18 years	£159.25
RD20C	Computerised Tomography Scan of One Area, without Contrast, 5 years and under	£104.27
PF	Plain Film (including x-ray)	£28.62

Direct access costs from NHS Reference costs: 2019-2020 version 2 ³⁴

1.1.11 Evidence statements

Economic

- One original comparative cost analysis conducted for the 2014 NICE Head Injury guideline, found that using the Canadian C-Spine rule for CT was the least costly strategy when compared to No imaging; CT all, Xray all; Canadian C-spine rule for Xray; NEXUS C-Spine rule for Xray and NEXUS C-Spine rule for CT for initial imaging for adults with suspected cervical spine injury and head injury. This analysis was assessed as partially applicable with potentially serious limitations.
- One original cost–utility analysis conducted for the 2016 NICE Spinal Injury guideline, found that Canadian C-Spine rule and CT was the cost-effective strategy compared to 17 other strategies for initial imaging for adults with suspected cervical spinal column injury and no other injuries. This analysis was assessed as partially applicable with potentially serious limitations.

1.1.12 The committee’s discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

Diagnostic accuracy

Diagnostic accuracy for any significant cervical spine injury (including fracture/bony injury, soft tissue/ligament damage, spinal cord injuries and vascular injuries) was relevant for the diagnostic accuracy component of this review. Sensitivity was considered the most important measure because the initial imaging method should pick up as many true positives as possible to avoid missing those with significant cervical spine injuries and subsequent negative consequences for the person with head injury and cervical spine injury, such as disability. It was noted that a high sensitivity contributes to management, as it provides reassurance that the test is good at ruling out injury and allowing early discharge or mobilisation. It was also noted that for imaging it is unlikely that many false positives will occur, so specificity values are generally higher than for other diagnostic tests or scoring systems, such as the clinical decision rules.

Diagnostic test and treat

For the diagnostic test and treat component of the review, all outcomes were considered equally important for decision-making and were primary outcomes, including all-cause mortality at 3 months, quality of life at ≥ 3 months, objectively reported scores of disability (such as the Glasgow Outcome Score or extended Glasgow Outcome Score) at ≥ 3 months, length of hospital stay, unscheduled readmission (28 days or longer) and neurological deterioration.

No studies comparing clinical outcomes between two different imaging strategies were identified.

1.1.12.2 The quality of the evidence

Possible population indirectness was present for most studies included in the review, as the proportion of people with confirmed head injury was not reported. The population was described only as those with suspected cervical spine injury undergoing imaging of the cervical spine. It was noted that many of those with cervical spine injury are likely to have experienced head injury based on the nature of the injury, for example those with whiplash are likely to have suffered a head injury as well. Therefore, the population of included studies varies, with few where it was clear all had confirmed or suspected head injury. Some studies included a population that was limited to those that were unconscious or obtunded, often requiring intensive care unit admission. Although head injury was not specifically mentioned in many studies, it was assumed that these groups did have at least suspected head injury given the severity of their injuries; these studies were not downgraded based on head injury not being mentioned.

Studies limiting to those more severely injured, only including people that were unconscious or obtunded, were however downgraded for indirectness. This is because the severe nature of their injuries makes them a very specific subgroup of the population that attend the emergency department with suspected cervical spine injury. Results would be less applicable than those of people who are discharged from the emergency department without admission to hospital or intensive care.

Reference standards used across studies differed. Many studies used 'final diagnosis' at discharge or including any readmissions as the reference standard, which was not always well-defined. Where studies had used this as the reference standard, if they had not included at least a 2-week period as part of the follow-up or this was unclear, this was taken into account when assessing indirectness. For studies that had used other reference standards listed in the protocol, for example CT or MRI where X-ray was used as the index test or CT and MRI combined for any index test, this was accepted and there was no reason to downgrade the reference standard for indirectness, regardless of whether or not there was a follow-up of 2 weeks. Similarly, a further factor considered in the risk of bias assessment for studies using final diagnosis as a reference standard was the fact that not all people included in the study had the same reference standard; for example, some may have had MRI while others did not.

Some studies did not use an external reference standard, but data was available to calculate the sensitivity of both CT and MRI when using CT and MRI combined as the reference standard; as this means that any person with a positive result on CT or MRI is considered to be reference standard-positive, false positives are not possible such that only sensitivity, and not specificity, can be calculated.

In terms of outcome definitions, some studies did report data for 'significant' cervical spine injuries, as specified in the protocol. However, some studies only reported any severity of cervical spine injury, not limiting to significant ones. Data from these studies was still included, but for studies reporting data for any severity and significant injuries, only data for the significant injuries was analysed as it is more relevant to the review protocol. A further way in which outcome definitions varied across studies was the types of injuries (for

example, bony or ligamentous/soft tissue) that were included. Some studies included any type of injury in the outcome/target condition whereas others focused the study on specific types of injuries, for example only fractures or only ligamentous injuries.

Given the differences between studies described above, pooling of results was not thought to be appropriate. Studies that were broadly similar in terms of index test, population, reference standard and target condition were grouped under the same headings but not formally pooled.

Most of the included evidence was very low quality based on the assessment of risk of bias, indirectness and a measure of imprecision for sensitivity and specificity. The exception was studies where head injury was clearly confirmed or suspected in studies, in which case the quality was low rather than very low. There were very few prospective studies, meaning many of the same issues were present in terms of risk of bias assessment.

- Some of the most common reasons that studies were downgraded for risk of bias included:
 - a consecutive sample not being enrolled or this being unclear
 - it being unclear if the index test and/or reference standard were interpreted without knowledge of the other
 - the interval between index test and reference standard being unclear
 - not all patients within a study having the same reference standard
- Indirectness was often present, with studies downgraded for one of the following reasons:
 - Head injury was not mentioned in the paper and included anyone with suspected cervical spine injury
 - They were very specific populations that may not be representative of the general population this review would apply to, including studies limiting specifically to those that were obtunded or unconscious with or without admission to an intensive care unit
 - Studies using 'final diagnosis' as a reference standard where it was unclear if a 2-week follow-up was incorporated into this standard, given that not all people received specific types of imaging such as MRI
- Imprecision was assessed separately for sensitivity and specificity. Thresholds of $\geq 90\%$ and $\geq 60\%$ for sensitivity and specificity, respectively, were used as values above which a test would be recommended and values of 0.7 and 0.4 below which a test is of no clinical use were set for sensitivity and specificity, respectively.

The limitations of the evidence were taken into account when considering any possible changes to existing recommendations. For children, these limitations contributed to the decision not to make any major changes to recommendations. Factors to consider for children include radiation exposure and risk of cancer. For adults, despite the limitations the committee agreed that the evidence supported the removal of X-ray as a primary imaging modality in people with head injury and suspected cervical spine injury. The committee agreed that current practice was already moving away from X-ray in adults and therefore although the evidence did have limitations it supported this change. Although it was unclear if many of the studies represented a head injury population, it was agreed that evidence from any people with suspected cervical spine injury is still relevant to the subgroup that also have head injury as many with suspected cervical spine injury are likely to have at least some type of head injury depending on the mechanism of injury.

1.1.12.3 Benefits and harms

Adults

Despite the limitations of the included evidence discussed in the previous section, including very few studies where it was clear the population had a head injury and methodology issues contributing to concerns about risk of bias, the committee were able to draw some conclusions from the evidence and use this to support decisions that were made.

The sensitivity values for X-ray in adult populations were consistently very low, with fourteen of sixteen analyses demonstrating values less than the 90% threshold specified in the protocol as a test that should be recommended and all fourteen of these studies having values also below 70%, with many below 50%. This included studies that reported any severity of injury and also those reporting clinically significant injuries. Where imprecision was present, this was because confidence intervals crossed the lower threshold of 70%, meaning even when considering confidence intervals, the sensitivity values for these studies could not be consistent with a value >90%. Results from one study reporting results separately for low-, moderate- and high-risk groups demonstrated that sensitivity was worse as the risk decreased; however, it was a very small study. For the two analyses where values >90% were reported, this included one very small analysis of 19 participants that were at high-risk and another was assessing the sensitivity of flexion-extension X-rays in those that had already been confirmed as CT-negative. This may represent secondary imaging rather than primary imaging and be less relevant to the review protocol. In both cases imprecision was also present, meaning the confidence intervals indicated uncertainty as to whether or not the true sensitivity value was >90%. Of the included studies, one of them was clearly in a suspected head injury population (as all had head CT) and the results for this study was one of those with a low sensitivity value for X-ray, which in this case was testing the ability to detect cervical spine fractures of any severity (32%; n=400; very low quality). Across all results for X-ray, specificity values were very good, with values >90% where they could be calculated.

In contrast, the committee noted that the sensitivity values for CT (for any severity of injury and clinically significant injuries) across studies were higher compared to X-ray. Across analyses using a reference standard other than CT+MRI combined (for example 'final diagnosis'), sensitivity values were all >90%, with fourteen of the eighteen analyses having values of 100%. This included one specific subgroup of intoxicated adults following blunt trauma (where it was unclear if head injury was present) where sensitivity was reported to be 93%, with imprecision present. The same study as above for X-ray also demonstrated that sensitivity values were 100% in low-, moderate- and high-risk groups for CT, though it was a very small study. Imprecision for sensitivity was present for some of the smaller studies, but there were some much larger studies (for example, two studies with ~10,000 people analysed) that also confirmed the high sensitivity values for CT of the cervical spine with no imprecision present. This improvement in sensitivity compared to X-ray did not come at the expense of specificity, as where reported these values were >90% in all but one analysis, with the other being 88%. It was noted that none of the studies discussed here for CT were clearly in a population with head injury or suspected head injury.

Studies where CT+MRI was used as a combined reference standard provided information about injuries that may be picked up on MRI but not on CT. This included three studies where it was clear head imaging had been performed in most or all people included and was therefore considered to be more relevant to the head injury population. Some reported any severity of injury while others reported unstable cervical spine injuries. Results demonstrated sensitivity values that were lower than those discussed in the previous paragraph, with all but one being lower than 90% (ranging from 71% to 100%). Using a combined reference standard of CT+MRI makes interpretation more difficult, as the lack of external reference standard makes it difficult to determine if a case missed on CT is a false negative on CT or a false positive on MRI. This is less of a problem where only unstable

injuries have been reported as this often requires an intervention. The committee noted that MRI may pick up ligamentous injuries that are not identified on CT, which may explain the lower sensitivity of CT when including results of MRI in the reference standard.

The only studies available for MRI as an index test in adults were those using combined CT+MRI as the reference standard, including three studies where it was clear head imaging had been performed in most or all people included and was therefore considered to be more relevant to the head injury population. The results were similar to those mentioned in the previous paragraph for CT, but there were five analyses reporting sensitivity values >90% rather than one (values ranged from 71% to 100%). Some reported any severity of injury while others reported unstable cervical spine injuries. These results suggest that some studies show that MRI picks up all injuries that were identified on CT, while others suggest it misses some identified on CT. The lack of results for MRI using an external reference standard, for example 'final diagnosis' as for CT and X-ray index tests discussed above, means the evidence identified for MRI as the initial imaging method in those with suspected cervical spine injury is more limited.

Based on the information discussed in the previous paragraphs, clinical experience and knowledge of current practice, the committee agreed that X-ray should not be used as an initial imaging strategy for the cervical spine in adults with head injury due to its poor sensitivity compared to CT. This was further supported by the committee as they noted that it is being used less frequently in current practice for adults and they highlighted that it can be time-consuming and distracting, with multiple views often required which takes up time (up to 3-4 hours), possibly delays the diagnosis process. It was also noted that it can be technically difficult in some people, for example those with large shoulders, and inadequate X-rays then mean a CT is done anyway. The committee agreed that they considered the quality of CTs to be more reliable than X-ray. The evidence from the very small study showing worsening sensitivity values for X-ray as risk group reduced (low-, moderate- and high-risk) was cited, as it suggested that even though a group is lower risk for cervical spine injury, this does not mean the sensitivity of X-ray is adequate to pick up injuries. This meant that the recommendation for X-ray in the group that have neck pain or tenderness but no high-risk indications for a CT cervical spine was edited so that CT is also performed in this group of people and the recommendation for CT in those at high-risk was retained. Other recommendations were edited to remove mention of X-ray, given it is now not included as an initial imaging strategy for adults with suspected cervical spine injury. This was also supported by cost-effectiveness evidence, as discussed in a later section.

Based on evidence from one study showing the sensitivity of X-ray to be poor for detecting fractures in those with diffuse idiopathic skeletal hyperostosis (DISH) with low-energy trauma, the committee agreed that people with a condition predisposing them to a higher risk of injury to the cervical spine (for example, ankylosing spondylitis) should be included as an additional factor in the group with neck pain or tenderness but not high-risk indications for a CT cervical spine. This was also extrapolated and included in the respective recommendation for children.

The committee highlighted the role that MRI has in imaging of the cervical spine, but agreed that there is limited evidence and it is rarely used as the first imaging strategy for adults with suspected cervical spine injury, meaning it cannot be recommended as an initial imaging method. Recommendations about the use of MRI as an additional form of imaging in certain circumstances were retained from the previous version of the guideline.

Children

Although limitations associated with the evidence for children were similar to those identified for adults, the committee agreed that additional factors complicated the recommendations for children, including the fact that there are concerns about radiation exposure and the risk of cancer.

Similar to the results for adults, some of the results for X-ray as an index test in children also demonstrated sensitivity values <90%. However, there were fewer studies in children and the sensitivity values for X-ray were in general higher compared to the adult population (values of 62%, 83% and 100% across the three studies, compared to adults where sensitivity values were often <50%); however, two of the studies were also small, with <100 people included, and the other was larger with 495 people analysed. There were also no studies where it was clear head injury had been confirmed or was suspected. The two studies with lower sensitivity values were those reporting any severity of cervical spine injury, while the single study reporting unstable injuries reported 100% sensitivity. However, for all three studies there was imprecision was sensitivity, meaning there was uncertainty about the true sensitivity of X-ray in children. Of the three studies, two reported specificity values >90% while the other reported a very low specificity of 1.6%.

Results for CT across seven included studies, with one specific to head injury as only those with confirmed severe traumatic brain injury were included, demonstrated sensitivity values that were similar to those for adults; five of the seven analyses reported values of 100%, with the other two reporting values of 85% and 23%. The study reporting the very low value of 23% was assessing the ability of CT to pick up ligamentous injuries specifically, with MRI as the reference standard; as it is established that CT is less able to pick up ligamentous injuries this result was expected, and it was unclear how many of these injuries were clinically significant. As for the X-ray results, imprecision was present for these sensitivity values meaning there was uncertainty about the true sensitivity of CT in children. For specificity, where reported the values were high, with all being >80% and many being >90%.

Results for MRI across six included studies, with one specific to head injury as only those with confirmed severe traumatic brain injury were included, demonstrated sensitivity values that were similar to those discussed for CT in the previous paragraph; five of the six analyses reported values of 100%, with the other (the study with confirmed head injury) reporting a value of 80%. This included some studies reporting any severity of injury and others reporting unstable injuries. One study specifically reporting fractures also reported a value of 100%, even though MRI is usually better at picking up ligamentous injuries. As for the X-ray and CT results, imprecision was present for these sensitivity values meaning there was uncertainty about the true sensitivity of MRI in children. For specificity, where reported the values were high, with all but one being >70% and the other being lower at 45%.

Based on the information discussed in the previous paragraphs, clinical experience and knowledge of current practice, the committee agreed that there was insufficient evidence to change any of the existing recommendations for children. Although some evidence suggested sensitivity values <90% for X-ray in children, fewer studies reported this compared to adults and the values were higher than those observed for adults. CT performed well in terms of sensitivity for children, as with for adults, but concerns about radiation exposure and cancer risk is a factor that needs to be considered in children. Radiation risk of CT was described as the biggest drawback for using CT in children for assessing the cervical spine as the risk of radiation-induced tumours (for example, thyroid tumours) may be higher for children as their organs are rapidly developing. Although the committee noted that the evidence for this is based on forecasting tools and extrapolation of risks rather than actual data, it is a risk that should be considered in decision-making and balancing risks and benefits. MRI also demonstrated good sensitivity values across most studies, however the committee noted that limitations of MRI in children include the need for immobilisation and/or sedation of children, as it is a longer process than CT and X-ray and requires children to remain still. Additionally, there was no cost-effectiveness evidence available for children for any of the index tests.

As the evidence was limited and changing to CT or MRI rather than X-ray as initial imaging in children would lead to a large change in practice for children with head injury and suspected cervical spine injury, the committee did not make any changes to the recommendations for cervical spine imaging in children; CT was retained only for those at higher risk and X-ray

recommended for those with no high-risk indications for CT but neck pain or tenderness. The committee further noted that in their experience, clinically significant cervical spine injury in children is much rarer than for adults, which further supported the decision not to expand the use of CT in children any further as the risks of radiation were considered to outweigh any possible benefit in terms of picking up cervical spine injuries.

In terms of MRI, the committee noted that existing recommendations about MRI as an additional form of imaging in certain circumstances were not age-specific and also applied to children.

As for adults, people with a condition predisposing them to a higher risk of injury to the cervical spine (for example, axial spondylarthritis was also included as an additional factor in the group with neck pain or tenderness but no high-risk indications for a CT cervical spine. There was no evidence for this in children but the committee agreed that collagen vascular disease or osteogenesis imperfecta may be important factors in children, as ankylosing spondylitis is extremely uncommon. Although in the study the results showed poor sensitivity of X-ray, the recommendation for children was to X-ray these children, as this is the method of imaging agreed for those considered to have no high-risk factors for CT in children.

1.1.12.4 Cost effectiveness and resource use

CT and MRI scanning are generally more expensive than plain X-ray but sometimes it can be difficult and time-consuming to get the right views for X-ray of the neck.

The clinical evidence review showed that CT is significantly more sensitive at diagnosing spinal injuries although it involves a substantial dose of radiation. Since untreated spinal injury could lead to damage to the spinal cord, with serious implications for the patient's quality of life and long-term costs for the NHS, the use of more costly imaging could be cost effective, depending on the prevalence of spine injury in the head injury population.

Adults

No published economic evaluations were found but two previous NICE guideline models were identified.

The model from the previous head injury CG176 compared strategies that encompassed both the Canadian C-spine and NEXUS rules with plain X-ray or CT scan. The optimal strategy was labelled "CT according to Canadian C-Spine rule" but on close inspection there were fewer CT scans in this strategy than in the strategy labelled "X-ray according to Canadian C-Spine rule for CT". This is due to the specificity of CT being misapplied in the model and due to the assumption in both strategies that 50% of false negatives get the other imaging modality. For this reason, the base case analysis of the model is fatally flawed. However, there was a sensitivity analysis 'GDG (guideline development group) estimates for initial imaging decisions', where the proportions having each test are far more plausible and reflect better the diagnostic accuracy evidence. The result of this sensitivity analysis (and the base case analysis) was that CT according to the Canadian C-spine rule was dominant – it had the lowest cost and the fewest false negatives. This model had some other limitations, for example the costs were for the initial hospital episode, not the long-term cost, although litigation costs were included in a sensitivity analysis.

The model from the NICE spinal injury guideline (NG41) also compared strategies that encompassed both the Canadian C-spine and NEXUS rules with plain X-ray, CT scan or MRI. Although the model population specified was suspected c-spine injury and no other injury, the diagnostic accuracy evidence base overlaps a great deal. The strategy that used CT according to the Canadian C-Spine rule was the most cost-effective yielding both the lowest long-term NHS cost and the most QALYs. This model had some limitations, for example the risk of spinal injury deterioration was based on expert opinion. Also, the

sensitivity of x-ray seems to be higher than the estimates found in the current guideline review, whereas the specificity seems to be a bit lower.

Both guideline models support the use of CT scanning over plain x-ray overall. However, they did not explicitly model the previous guideline recommendations, which are CT for high-risk patients and X-ray for moderate risk. This was recommended by the previous guideline committee because they were concerned about the resource implications of referring everyone for CT, the exposure to radiation and the relatively poor specificity of the C-spine prediction rules. Modelling of that strategy does not seem to be possible because of the lack of data on the prevalence of c-spine injury in the moderate risk population.

Although there is some uncertainty around the cost effectiveness of extending CT scanning to adults who are assessed as moderate risk of cervical spine injury, the committee decided to recommend CT because of its much greater sensitivity and because it has become current practice for adults in recent years.

Children

No economic evaluations were found.

Given concerns about radiation exposure to the thyroid in children and insufficient evidence about the diagnostic accuracy of MRI, the committee decided not to change the recommendations for children and therefore plain x-ray was retained for children identified as at moderate risk. The cost effectiveness of this strategy is uncertain but since the committee were not considering moving away from current practice there is not a cost impact.

1.1.12.5 Other factors the committee took into account

Some additional changes to recommendations were made that were not based on the content of the evidence review, which included removing some older recommendations that were no longer seen as necessary given they are now all carried out routinely anyway. Recommendations on when to carry out full cervical spine immobilisation were removed as there is a guideline on spinal injury which should be referred to.

Other edits included editing the wording for clarity. This included making it clear that MRI recommended if there are neurological signs and symptoms referable to the cervical spine would be subsequent imaging, for example following CT or X-ray, and would not be as an initial form of imaging.

Another edit was made to one of the factors listed as a high-risk indicator for CT in adults and children; the example given for when 'a definitive diagnosis of cervical spine injury is needed urgently' was edited from 'before surgery' to explain further, with manipulation of the cervical spine being requiring during surgery or anaesthesia being added.

The committee were aware of the Denver criteria for CT angiography of the neck but these were not relevant to the review protocol.

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Appendices

Appendix A – Review protocols

Review protocol for CT, MRI and X-ray of the cervical spine in people with head injury – diagnostic accuracy

ID	Field	Content
0.	PROSPERO registration number	CRD42021283523
1.	Review title	What is the diagnostic accuracy of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?
2.	Review question	What is the diagnostic accuracy of CT , MRI and X-ray of the cervical spine for initial imaging in people with head injury?
3.	Objective	To determine which of the currently available imaging techniques is best to diagnose cervical spine injury.
4.	Searches	<p>The following databases (from inception) will be searched:</p> <ul style="list-style-type: none"> • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> • English language studies • Human studies • Letter and comments excluded

		<p>Other searches:</p> <ul style="list-style-type: none"> • [Inclusion lists of systematic reviews] <p>The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant.</p> <p>The full search strategies will be published in the final review.</p> <p>Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).</p>
5.	Condition or domain being studied	Cervical spine injury in patients who have experienced a head injury.
6.	Population	<p>Inclusion: Infants, children and adult with head injury and suspected cervical spine injury</p> <p>Strata:</p> <ul style="list-style-type: none"> • Adults at: <ul style="list-style-type: none"> ○ high risk ○ moderate risk ○ low risk • Children + infants at: <ul style="list-style-type: none"> ○ high risk ○ moderate risk

		<ul style="list-style-type: none"> ○ low risk • Adults (aged ≥16 years) • Children and infants (aged 0 to <16 years). <p>Mixed population studies will be included but downgraded for indirectness. Cut-off of 60% will be used for all age groups</p> <p>Exclusion: Adults, and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury.</p> <p>C spine injury risk stratification based on:</p> <ul style="list-style-type: none"> • Canadian C Spine Rule • NEXUS <p>Stratification rules should be kept separate as they have different features.</p> <p>Both for adults and children. Both rules validated in adults and extrapolated for children. These are not specific for head injury .</p>
7.	Test	<ul style="list-style-type: none"> • Computed tomography scan (CT) of cervical spine • Magnetic resonance imaging (MRI) of cervical spine • X-ray of cervical spine
8.	Reference standard	<p>For diagnostic accuracy:</p> <p><u>Reference standard for CT:</u></p> <ul style="list-style-type: none"> • CT and MR imaging of cervical spine <p>Or</p>

		<ul style="list-style-type: none"> • 2 weeks follow-up after CT including autopsy findings <p><u>Reference standard for MR imaging:</u></p> <ul style="list-style-type: none"> • CT and MR imaging of cervical spine <p style="text-align: center;">Or</p> <ul style="list-style-type: none"> • 2 weeks follow-up after MR imaging including autopsy findings <p><u>Reference standard for X-ray:</u></p> <ul style="list-style-type: none"> • CT or MR imaging of cervical spine <p style="text-align: center;">Or</p> <ul style="list-style-type: none"> • CT and MRI imaging of cervical spine <p style="text-align: center;">or</p> <ul style="list-style-type: none"> • 2 weeks follow-up after X-ray including autopsy findings <p>For X-ray only include children and people below 65 years. People >65 years are considered as high risk and will be offered CT cervical spine within 8 hours of injury (CG 176). Vascular injuries will be picked up by MR imaging</p>
9.	Types of study to be included	<p>Diagnostic accuracy: Diagnostic cross-sectional studies, cohort studies (prospective and retrospective)</p>

		Systematic reviews and meta-analyses of the above
10.	Other exclusion criteria	<p>Non-English language studies.</p> <p>Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.</p>
11.	Context	<p>Head-injured patient may also have sustained concomitant injury to the cervical spine. Some head injured patients who require a CT head scan will also need cervical spine imaging. The purpose of this review is to inform the optimal diagnostic pathways for these patients using the best evidence available.</p>
12.	Primary outcomes (critical outcomes)	<p>All outcomes are considered equally important for decision making and therefore have all been rated as critical:</p> <p>Diagnostic accuracy outcomes</p> <ul style="list-style-type: none"> • Diagnostic accuracy CT, MRI and X-ray of the cervical spine for any significant cervical spine injury (fracture/bony injury, soft tissue/ligament damage, spinal cord injuries, vascular injuries) <p>No objective definition for significant cervical spine injury. Note definitions as reported in the papers.</p> <p>Diagnostic test accuracy to be reported by test sensitivity/specificity</p> <p>For measurement of imprecision, clinical decision thresholds for sensitivity and specificity are set at 90% and 60%.</p> <p>Sensitivity is considered to be more important than specificity. Sensitivity is more important as that will change management. Often, the decision is whether</p>

		<p>someone can be discharged from ED. A test with high sensitivity that is negative is very reassuring in ruling out an injury and allowing early discharge or mobilisation. It's unlikely that imaging will produce false positives (i.e. low specificity).</p> <p>COMET database was searched for relevant core outcome sets and none were identified.</p>
13.	Data extraction (selection and coding)	<p>All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated.</p> <p>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>This review will make use of the priority screening functionality within the EPPI-reviewer software.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above.</p> <p>A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).</p> <p>10% of all evidence reviews are quality assured by a senior research fellow. This includes checking:</p> <ul style="list-style-type: none"> • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments <p>Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.</p>

14.	Risk of bias (quality) assessment	<p>For diagnostic reviews</p> <ul style="list-style-type: none"> • Diagnostic test accuracy studies: QUADAS-2 	
15.	Strategy for data synthesis	<p>For diagnostic accuracy evidence:</p> <ul style="list-style-type: none"> • Aggregate data on diagnostic accuracy of investigations will be collected and synthesized in a quantitative data analysis. • Endnote will be used for bibliography, citations, sifting and reference management. <p>WinBUGS will be used for meta-analysis of diagnostic accuracy studies if included studies are sufficiently homogeneous.</p>	
16.	Analysis of sub-groups	<p>Subgroups that will be investigated if heterogeneity is present:</p> <p>Types of injuries:</p> <ul style="list-style-type: none"> • Bone injuries • Spinal cord injuries • other soft tissue injuries • vascular injuries 	
17.	Type and method of review	<input type="checkbox"/>	Intervention
		<input checked="" type="checkbox"/>	Diagnostic
		<input type="checkbox"/>	Prognostic

		<input type="checkbox"/>	Qualitative	
		<input type="checkbox"/>	Epidemiologic	
		<input type="checkbox"/>	Service Delivery	
		<input type="checkbox"/>	Other (please specify)	
18.	Language	English		
19.	Country	England		
20.	Anticipated or actual start date			
21.	Anticipated completion date			
22.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Piloting of the study selection process	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Formal screening of search results against eligibility criteria	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Data extraction	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Risk of bias (quality) assessment	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Data analysis	<input type="checkbox"/>	<input checked="" type="checkbox"/>
23.	Named contact	5a. Named contact National Guideline Centre		

		<p>5b Named contact e-mail headinjury@nice.org.uk</p> <p>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Centre</p>
24.	Review team members	<p>From the National Guideline Centre:</p> <p>Guideline lead: Sharon Swain</p> <p>Senior systematic reviewer: Sharangini Rajesh</p> <p>Senior systematic reviewer: Julie Neilson</p> <p>Health economist: David Wonderling</p> <p>Information specialist: Joseph Runicles</p> <p>Project manager: Giulia Zuodar</p>
25.	Funding sources/sponsor	<p>This systematic review is being completed by the National Guideline Centre which receives funding from NICE.</p>
26.	Conflicts of interest	<p>All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.</p>

27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual . Members of the guideline committee are available on the NICE website: 1 (nice.org.uk) .	
28.	Other registration details		
29.	Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=283523	
30.	Dissemination plans	<p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. 	
31.	Keywords	head injury	
32.	Details of existing review of same topic by same authors	[Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible. NOTE: most NICE reviews will not constitute an update in PROSPERO language. To be an update it needs to be the same review question/search/methodology. If anything has changed it is a new review]	
33.	Current review status	<input type="checkbox"/>	Ongoing
		<input checked="" type="checkbox"/>	Completed but not published
		<input type="checkbox"/>	Completed and published
		<input type="checkbox"/>	Completed, published and being updated
		<input type="checkbox"/>	Discontinued

34.	Additional information	
35.	Details of final publication	www.nice.org.uk

Review protocol for CT, MRI and X-ray of the cervical spine in people with head injury – diagnostic accuracy

ID	Field	Content
0.	PROSPERO registration number	CRD42021283526
1.	Review title	What is the clinical and cost effectiveness of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?
2.	Review question	What is the clinical and cost effectiveness of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?
3.	Objective	To determine which of the currently available imaging techniques is best to diagnose cervical spine injury.
4.	Searches	<p>The following databases (from inception) will be searched:</p> <ul style="list-style-type: none"> • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> • English language studies • Human studies • Letter and comments excluded

		<p>Other searches:</p> <ul style="list-style-type: none"> • [Inclusion lists of systematic reviews] <p>The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant.</p> <p>The full search strategies will be published in the final review.</p> <p>Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).</p>
5.	Condition or domain being studied	Cervical spine injury in patients who have experienced a head injury.
6.	Population	<p>Inclusion: Infants, children and adult with head injury and suspected cervical spine injury</p> <p>Strata:</p> <ul style="list-style-type: none"> • Adults at: <ul style="list-style-type: none"> ○ high risk ○ moderate risk ○ low risk • Children + infants at: <ul style="list-style-type: none"> ○ high risk ○ moderate risk

		<ul style="list-style-type: none"> ○ low risk • Adults (aged ≥16 years) • Children and infants (aged 0 to <16 years). <p>Mixed population studies will be included and downgraded for indirectness. Cut-off of 60% will be used for all age groups.</p> <p>Exclusion: Adults, and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury.</p> <p>C spine injury risk stratification based on:</p> <ul style="list-style-type: none"> • Canadian C Spine Rule • NEXUS <p>Stratification rules should be kept separate as they have different features</p> <p>Both for adults and children. Both rules validated in adults and extrapolated for children. These are not specific for head injury</p>
7.	Intervention	<ul style="list-style-type: none"> • Computed tomography scan (CT) of cervical spine • Magnetic resonance imaging (MRI) of cervical spine • X-ray of cervical spine
8.	comparator	<p>MRI of cervical spine, X-ray of cervical spine and CT of cervical spine compared to each other</p> <p>For X-ray only include children and people below 65 years.</p> <p>People >65 years are considered as high risk and will be offered CT cervical spine within 8 hours of injury (CG 176).</p> <p>Vascular injuries will be picked up by MR imaging</p>

9.	Types of study to be included	<p>Diagnostic test and treat:</p> <ul style="list-style-type: none"> • Randomised controlled trials (RCTs), systematic reviews of RCTs. • If no RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders, starting with prospective cohort studies. <p>Key confounders</p> <ul style="list-style-type: none"> • Age • Gender • GCS or pupillary response at presentation
10.	Other exclusion criteria	<p>Non-English language studies.</p> <p>Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.</p>
11.	Context	<p>Head-injured patient may also have sustained concomitant injury to the cervical spine. Some head injured patients who require a CT head scan will also need cervical spine imaging. The purpose of this review is to inform the optimal diagnostic pathways for these patients using the best evidence available.</p>
12.	Primary outcomes (critical outcomes)	<p>All outcomes are considered equally important for decision making and therefore have all been rated as critical:</p> <ul style="list-style-type: none"> • Mortality at 3 months

		<ul style="list-style-type: none"> • Quality of life - 3 months or more • Objectively applied score of disability e.g. Glasgow Outcome Score (GOS) or extended GOS - at 3 months or more • Length of hospital stay • Unscheduled re-admission (28 days or longer) • Neurological deterioration <p>Neurological deterioration could be because of either no imaging or no appropriate imaging.</p> <p>Spinal injuries are determined by different scales– e.g. American Spinal Injury Association (ASIA), functional independence measure (FIM). Different scales are used. Report as in the studies</p> <p>Vascular insult would be picked up in outcome neurological deterioration</p> <p>COMET database was searched for relevant core outcome sets and none were identified.</p>
13.	Data extraction (selection and coding)	<p>All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated.</p> <p>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>This review will make use of the priority screening functionality within the EPPI-reviewer software.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above.</p> <p>A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).</p>

		<p>10% of all evidence reviews are quality assured by a senior research fellow. This includes checking:</p> <ul style="list-style-type: none"> • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments <p>Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.</p>
14.	Risk of bias (quality) assessment	<p>For diagnostic Test and treat:</p> <ul style="list-style-type: none"> • Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • For Intervention reviews <ul style="list-style-type: none"> • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) • Non randomised study, including cohort studies: Cochrane ROBINS-I
15.	Strategy for data synthesis	<p>For diagnostic test and treat:</p> <ul style="list-style-type: none"> • Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to

		<p>calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences.</p> <ul style="list-style-type: none"> Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ <p>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.</p>	
16.	Analysis of sub-groups	<p>Subgroups that will be investigated if heterogeneity is present:</p> <p>Types of injuries:</p> <ul style="list-style-type: none"> Bone injuries Spinal cord injuries other soft tissue injuries vascular injuries 	
17.	Type and method of review	<input checked="" type="checkbox"/>	Intervention

		<input type="checkbox"/>	Diagnostic	
		<input type="checkbox"/>	Prognostic	
		<input type="checkbox"/>	Qualitative	
		<input type="checkbox"/>	Epidemiologic	
		<input type="checkbox"/>	Service Delivery	
		<input type="checkbox"/>	Other (please specify)	
18.	Language	English		
19.	Country	England		
20.	Anticipated or actual start date			
21.	Anticipated completion date			
22.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Piloting of the study selection process	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Formal screening of search results against eligibility criteria	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Data extraction	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Risk of bias (quality) assessment	<input type="checkbox"/>	<input checked="" type="checkbox"/>
		Data analysis	<input type="checkbox"/>	<input checked="" type="checkbox"/>

23.	Named contact	<p>5a. Named contact National Guideline Centre</p> <p>5b Named contact e-mail headinjury@nice.org.uk</p> <p>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Centre</p>
24.	Review team members	<p>From the National Guideline Centre:</p> <p>Guideline lead: Sharon Swain</p> <p>Senior systematic reviewer: Sharangini Rajesh</p> <p>Senior systematic reviewer: Julie Neilson</p> <p>Health economist: David Wonderling</p> <p>Information specialist: Joseph Runicles</p> <p>Project manager: Giulia Zuodar</p>
25.	Funding sources/sponsor	<p>This systematic review is being completed by the National Guideline Centre which receives funding from NICE.</p>
26.	Conflicts of interest	<p>All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the</p>

		development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual . Members of the guideline committee are available on the NICE website: 1 (nice.org.uk) .	
28.	Other registration details		
29.	Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=283526	
30.	Dissemination plans	<p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. 	
31.	Keywords	Head injury	
32.	Details of existing review of same topic by same authors		
33.	Current review status	<input type="checkbox"/>	Ongoing
		<input checked="" type="checkbox"/>	Completed but not published
		<input type="checkbox"/>	Completed and published
		<input type="checkbox"/>	Completed, published and being updated

		<input type="checkbox"/>	Discontinued
34.	Additional information		
35.	Details of final publication		www.nice.org.uk

Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	<ul style="list-style-type: none"> • Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. The search covered all years
Review strategy	<p>Studies not meeting any of the search criteria above will be excluded. Studies published before 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.</p> <p>Studies published in 2006 or later that were included in the previous guidelines will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified.</p> <p>Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).³²</p> <p>Inclusion and exclusion criteria</p>

- If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile.
- If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.
- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2006 or later (including any such studies included in the previous guidelines) but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as 'Not applicable'.
- Studies published before 2006 (including any such studies included in the previous guidelines) will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B – Literature search strategies

This literature search strategy was used for the following questions:

- What is the diagnostic accuracy of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?
- What is the clinical and cost effectiveness of CT, MRI and X-ray of the cervical spine for initial imaging in people with head injury?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.³²

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve.

Table 29: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
The Cochrane Library (Wiley)	Cochrane Reviews to 2022 Issue 6 of 12 CENTRAL to 2022 Issue 6 of 12	

Medline (Ovid) search terms

1.	exp Spinal Injuries/
2.	Spinal Cord Injuries/
3.	exp Neck Injuries/
4.	whiplash.ti,ab.
5.	((neck or spine or spinal) adj3 (trauma or injur* or fracture*)).ti,ab.
6.	or/1-5
7.	cervical.ti,ab.
8.	6 and 7
9.	(cervical adj3 (trauma* or injur* or fracture*)).ti,ab.
10.	8 or 9
11.	letter/

12.	editorial/
13.	news/
14.	exp historical article/
15.	Anecdotes as Topic/
16.	comment/
17.	case report/
18.	(letter or comment*).ti.
19.	or/11-18
20.	randomized controlled trial/ or random*.ti,ab.
21.	19 not 20
22.	animals/ not humans/
23.	exp Animals, Laboratory/
24.	exp Animal Experimentation/
25.	exp Models, Animal/
26.	exp Rodentia/
27.	(rat or rats or mouse or mice or rodent*).ti.
28.	or/21-27
29.	10 not 28
30.	limit 29 to English language
31.	tomography/
32.	exp magnetic resonance imaging/
33.	exp tomography, emission-computed/
34.	exp tomography, x-ray/
35.	Radiography/
36.	Neuroradiography/
37.	(compute* adj2 tomograph*).ti,ab.
38.	(CT or CAT or PET or SPECT).ti,ab.
39.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph*)).ti,ab.
40.	MRI.ti,ab.
41.	(radiograph* or xray* or x-ray* or x ray*).ti,ab.
42.	or/31-41
43.	30 and 42

Embase (Ovid) search terms

1.	spine injury/
2.	cervical spine injury/
3.	spinal cord injury/
4.	cervical spinal cord injury/
5.	neck injury/
6.	whiplash injury/
7.	whiplash.ti,ab.
8.	((neck or spine or spinal) adj3 (trauma or injur*)).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.

12.	editorial.pt.
13.	(conference abstract or conference paper).pt.
14.	case report/ or case study/
15.	(letter or comment*).ti.
16.	or/10-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animal/ not human/
20.	nonhuman/
21.	exp Animal Experiment/
22.	exp Experimental Animal/
23.	animal model/
24.	exp Rodent/
25.	(rat or rats or mouse or mice or rodent*).ti.
26.	or/18-25
27.	9 not 26
28.	limit 27 to English language
29.	tomography/
30.	brain tomography/
31.	exp computer assisted tomography/
32.	exp emission tomography/
33.	exp nuclear magnetic resonance imaging/
34.	radiography/
35.	(compute* adj2 tomograph*).ti,ab.
36.	(CT or CAT or PET or SPECT).ti,ab.
37.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph* or angiograph*)).ti,ab.
38.	MRI.ti,ab.
39.	(radiograph* or xray* or x-ray* or x ray*).ti,ab.
40.	neuroradiology/ or brain radiography/
41.	or/29-40
42.	28 and 41

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Spinal Injuries] explode all trees
#2.	MeSH descriptor: [Spinal Cord Injuries] this term only
#3.	MeSH descriptor: [Neck Injuries] explode all trees
#4.	whiplash:ti,ab
#5.	((neck or spine or spinal) near/3 (trauma or injur* or fracture*)):ti,ab
#6.	#1 or #2 or #3 or #4 or #5
#7.	cervical:ti,ab
#8.	#6 and #7
#9.	(cervical near/3 (trauma* or injur* or fracture*)):ti,ab
#10.	#8 or #9
#11.	MeSH descriptor: [Tomography] this term only
#12.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees

#13.	MeSH descriptor: [Tomography, Emission-Computed] explode all trees
#14.	MeSH descriptor: [Tomography, X-Ray] explode all trees
#15.	MeSH descriptor: [Radiography] this term only
#16.	MeSH descriptor: [Neuroradiography] this term only
#17.	(compute* near/2 tomograph*):ti,ab
#18.	(CT or CAT or PET or SPECT):ti,ab
#19.	((MR or magnetic resonance or NMR) near/2 (imag* or tomograph* or angiograph*)):ti,ab
#20.	MRI:ti,ab
#21.	(radiograph* or xray* or x-ray* or x ray*):ti,ab
#22.	#11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21
#23.	#10 and #22

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting searches using terms for a broad Head Injury population. The following databases were searched: NHS Economic Evaluation Database (NHS EED - this ceased to be updated after 31st March 2015), Health Technology Assessment database (HTA - this ceased to be updated from 31st March 2018) and The International Network of Agencies for Health Technology Assessment (INAHTA). Searches for recent evidence were run on Medline and Embase from 2014 onwards for health economics, and all years for quality-of-life studies.

Table 30: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies
	Quality of Life 1946 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports)
		English language
Embase (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies
	Quality of Life 1974 – 22 June 2022	Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts)
		English language
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception – 31 st March 2015	
Health Technology Assessment Database (HTA)	Inception – 31 st March 2018	

Database	Dates searched	Search filters and limits applied
(Centre for Research and Dissemination – CRD)		
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception – 22 June 2022	English language

Medline (Ovid) search terms

1.	craniocerebral trauma/ or exp brain injuries/ or coma, post-head injury/ or exp head injuries, closed/ or head injuries, penetrating/ or exp intracranial hemorrhage, traumatic/ or exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab.
3.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.
5.	or/1-4
6.	letter/
7.	editorial/
8.	news/
9.	exp historical article/
10.	Anecdotes as Topic/
11.	comment/
12.	case report/
13.	(letter or comment*).ti.
14.	or/6-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animals/ not humans/
18.	exp Animals, Laboratory/
19.	exp Animal Experimentation/
20.	exp Models, Animal/
21.	exp Rodentia/
22.	(rat or rats or mouse or mice or rodent*).ti.
23.	or/16-22
24.	5 not 23
25.	limit 24 to English language
26.	economics/
27.	value of life/
28.	exp "costs and cost analysis"/
29.	exp Economics, Hospital/
30.	exp Economics, medical/
31.	Economics, nursing/

32.	economics, pharmaceutical/
33.	exp "Fees and Charges"/
34.	exp budgets/
35.	budget*.ti,ab.
36.	cost*.ti.
37.	(economic* or pharmaco?economic*).ti.
38.	(price* or pricing*).ti,ab.
39.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
40.	(financ* or fee or fees).ti,ab.
41.	(value adj2 (money or monetary)).ti,ab.
42.	or/26-41
43.	quality-adjusted life years/
44.	sickness impact profile/
45.	(quality adj2 (wellbeing or well being)).ti,ab.
46.	sickness impact profile.ti,ab.
47.	disability adjusted life.ti,ab.
48.	(qal* or qtime* or qwb* or daly*).ti,ab.
49.	(euroqol* or eq5d* or eq 5*).ti,ab.
50.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/32-61
63.	25 and (42 or 62)

Embase (Ovid) search terms

1.	head injury/
2.	exp brain injury/
3.	skull injury/ or exp skull fracture/
4.	((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)).ti,ab.
5.	((skull or cranial) adj3 fracture*).ti,ab.
6.	(trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.

7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	(conference abstract or conference paper).pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	or/8-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	health economics/
28.	exp economic evaluation/
29.	exp health care cost/
30.	exp fee/
31.	budget/
32.	funding/
33.	budget*.ti,ab.
34.	cost*.ti.
35.	(economic* or pharmaco?economic*).ti.
36.	(price* or pricing*).ti,ab.
37.	(cost* adj2 (effectiv* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
38.	(financ* or fee or fees).ti,ab.
39.	(value adj2 (money or monetary)).ti,ab.
40.	or/27-39
41.	quality-adjusted life years/
42.	"quality of life index"/
43.	short form 12/ or short form 20/ or short form 36/ or short form 8/
44.	sickness impact profile/
45.	(quality adj2 (wellbeing or well being)).ti,ab.
46.	sickness impact profile.ti,ab.
47.	disability adjusted life.ti,ab.
48.	(qal* or qtime* or qwb* or daly*).ti,ab.

49.	(euroqol* or eq5d* or eq 5*).ti,ab.
50.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/41-61
63.	26 and (40 or 62)

NHS EED and HTA (CRD) search terms

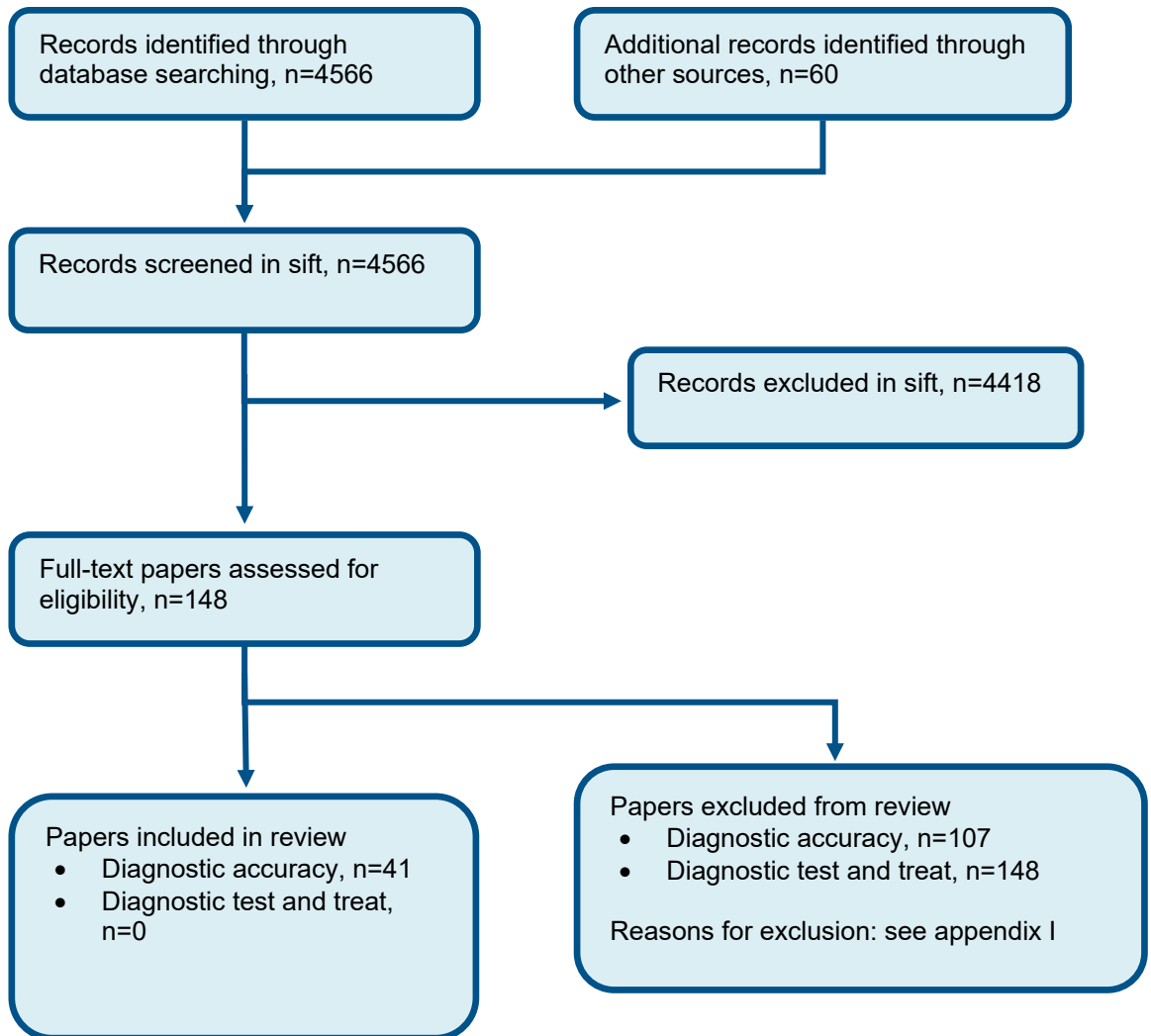
#1.	MeSH DESCRIPTOR Brain Injuries EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Craniocerebral Trauma
#3.	MeSH DESCRIPTOR Coma, Post-Head Injury
#4.	MeSH DESCRIPTOR Head Injuries, Closed EXPLODE ALL TREES
#5.	MeSH DESCRIPTOR Head Injuries, Penetrating
#6.	MeSH DESCRIPTOR Intracranial Hemorrhage, Traumatic EXPLODE ALL TREES
#7.	MeSH DESCRIPTOR Skull Fractures EXPLODE ALL TREES
#8.	(((skull or cranial) adj3 fracture*))
#9.	(((head or brain or craniocerebral or intracranial or cranial or skull) adj3 (injur* or trauma*)))
#10.	((trauma* and ((subdural or intracranial or brain) adj2 (h?ematoma* or h?emorrhage* or bleed*))))
#11.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10

INAHTA search terms

1.	(((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title] AND (((trauma* and ((subdural or intracranial or brain) and (haematoma* or hematoma* or haemorrhage* or hemorrhage* or bleed*))))[Title]) OR (((skull or cranial) and fracture*)[Title] OR (((skull or cranial) and fracture*)[abs]) OR (((head or brain or craniocerebral or intracranial or cranial or skull) and (injur* or trauma*))[Title] OR ((head or brain or craniocerebral or intracranial or cranial or skull) and (injur* or trauma*))[abs]) OR ("Skull Fractures"[mhe]) OR ("Intracranial Hemorrhage, Traumatic"[mhe]) OR ("Head Injuries, Penetrating"[mh]) OR ("Head Injuries, Closed"[mhe]) OR ("Coma, Post-Head Injury"[mh]) OR ("Brain Injuries"[mhe]) OR ("Craniocerebral Trauma"[mh])
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Appendix C –Diagnostic evidence study selection

Figure 1: Flow chart of clinical study selection for the review of CT, MRI and X-ray of the cervical spine in people with head injury



Appendix D Diagnostic evidence

Note that some evidence tables may contain outcomes that were not eventually included in the analysis, for example for studies that reported both any severity of cervical spine injury and clinically significant/unstable injuries separately, the latter was used for analysis and the results for any injury severity not used as this was closest to the target condition in the protocol.

D.1 Adults

Reference	Adams 2006¹
Study type	Retrospective chart review
Study methodology	Data source: chart review of CT and MRI reports and changes in clinical management as part of Morristown Memorial Hospital Trauma Quality Improvement Initiative Recruitment: records of those within a 12 month period (January 1 st 2004 to December 31 st 2004) matching inclusion criteria were included
Number of patients	n = 97 (n=99 undergoing MRI cervical spine identified and n=97 charts were complete and available for review)
Patient characteristics	Age, mean (SD): 40 (21) years Gender (male to female ratio): 71.1% male and 28.9% female Ethnicity: not reported

Reference	Adams 2006 ¹
	<p data-bbox="546 229 1749 261">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="546 347 1722 379">Injury severity score, mean (SD): 15 (11) in whole population and 24 (9) in obtunded group</p> <p data-bbox="546 466 819 497">Mechanism of injury:</p> <ul data-bbox="595 523 976 660" style="list-style-type: none"><li data-bbox="595 523 976 555">• Motor vehicle crash, 45%<li data-bbox="595 560 786 592">• Falls, 44%<li data-bbox="595 596 931 628">• Pedestrian struck, 6%<li data-bbox="595 633 815 665">• Assaults, 4% <p data-bbox="546 746 1180 778">Setting: secondary care – hospital/trauma centre</p> <p data-bbox="546 865 730 896">Country: USA</p> <p data-bbox="546 983 1995 1046">Inclusion criteria: underwent MRI cervical spine trauma protocol; deemed high-risk for axial trauma due to pain, neurologic symptoms or obtundation after significant blunt trauma; and complete chart data available for review.</p> <p data-bbox="546 1129 945 1161">Exclusion criteria: not reported</p> <p data-bbox="546 1248 1518 1279">Adults with high suspicion of axial trauma undergoing MRI of cervical spine</p>

Reference	Adams 2006¹
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided (assumed head injury based on severity of injuries – all at high suspicion of axial trauma)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>Performed using GE light speed 4-slice CT scanner with collimation of 5 mm, pitch of 1.6. and reconstructions at 1 mm of image spacing from base of skull to first thoracic vertebrae.</p> <p><u>Reference standard</u></p> <p>Final diagnosis based on MRI and CT and clinical decision-making of spinal consultants, no follow-up mentioned.</p> <p>MRI of cervical spine performed without contrast. Sagittal T1- and T2-weighted images acquired from posterior fossa through 5th thoracic vertebrae. 3 mm thin section contiguous axial and sagittal T1- and T2-weighted images obtained from 2nd cervical vertebrae through 1st thoracic vertebrae. When available, comparison was made with the CT of cervical spine by attending radiologist.</p> <p>All imaging studies evaluated based on radiology department protocols. After initial review by radiology residents, attending radiologist then read studies. No attempt at blinding radiology staff to results of CT or MRI was made and final printed radiology report accepted as official reading of the study. Presence or absence of acute spinal injury based on official MRI and CT scan reports and clinical decision-making of spinal consultants. Areas of discrepancy between CT and MRI were subjected to formal interrogation by dedicated thin cut CT imaging on the level in question.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and subsequent tests/final confirmed diagnosis</p>
Outcome	Cervical spine injury – poorly defined

Reference	Adams 2006¹
2x2 table	Raw data not reported to allow 2x2 tables to be calculated
Statistical measures	<p>Cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 94.0%</p> <p>Specificity: 88.0%</p> <p>PPV: NR</p> <p>NPV: NR</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, index test and reference standard likely interpreted with knowledge of the other, unclear time interval between index test and reference standard and unclear if reference standard components differed between patients</p> <p>Indirectness: very serious – all included were at high-risk/more severely injured which may be less applicable to general population of those attending ED with suspected cervical spine injury, and reference standard possibly places focus on MRI results with it also unclear if follow-up included 2 weeks</p>
Comments	None

Reference	Bailitz 2009³
Study type	Prospective observational study
Study methodology	Data source: conducted at single hospital trauma unit Recruitment: consecutive patients presenting to Cook County Hospital Trauma Unit meeting inclusion criteria between December 15 th 2004 and November 15 th 2006.
Number of patients	n = 1505 (n=1583 had cervical spine trauma and n=78 patients were excluded as they did not have both CT and radiography, leaving n=1505 patients)
Patient characteristics	Age, mean (SD): 37 (SD not reported) years Gender (male to female ratio): 72% male and 28% female Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: <ul style="list-style-type: none"> • Motor vehicle collisions, 40% • Assault, 25% • Fall, 20% • Pedestrian struck by car, 9%

Reference	Bailitz 2009³
	<p>Setting: secondary care – hospital trauma unit</p> <p>Country: USA</p> <p>Inclusion criteria: meeting at least one of NEXUS criteria and therefore requiring cervical spine imaging for vertebral bone blunt cervical trauma injury (criteria were: midline pain or tenderness, neurologic findings, altered mental status, intoxication and distracting injury); and had both CT and X-ray performed.</p> <p>Exclusion criteria: <16 years</p> <p>People meeting at least one NEXUS criterion and suspicion of cervical spine injury – CT and X-ray performed</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine – three-view</p> <p>CT of cervical spine</p> <p>Final readings for index tests were performed by two attending radiologists provided with same basic clinical information while blinded to the results of other imaging study and earlier preliminary readings. No further details provided for index tests</p>

Reference	Bailitz 2009³																														
	<p><u>Reference standard</u></p> <p>Final diagnosis in medical record at discharge</p> <p>Time between measurement of index test and reference standard: unclear time interval between index tests and subsequent tests/final confirmed diagnosis</p>																														
Outcome	<p>Clinically significant cervical spine injury – reported separately for different risk strata (NEXUS) as in protocol</p> <p>Clinically significant injuries were defined as those requiring one or more of following interventions recommended by neurosurgical consultation: operative procedure, halo application and/or rigid cervical collar.</p>																														
2x2 table	<p>Clinically significant cervical spine injury – X-ray as index test (high risk)</p> <table border="1" data-bbox="530 738 1610 1066"> <thead> <tr> <th></th> <th>Reference standard +</th> <th>Reference standard -</th> <th>Total</th> <th rowspan="4">Raw data reported insufficiently meaning specificity could not be calculated and is not reported</th> </tr> </thead> <tbody> <tr> <td>Index test +</td> <td>7</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>Index test -</td> <td>8</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>Total</td> <td>15</td> <td>NR</td> <td>NR</td> </tr> </tbody> </table> <p>Clinically significant cervical spine injury – X-ray as index test (moderate risk)</p> <table border="1" data-bbox="530 1129 1610 1276"> <thead> <tr> <th></th> <th>Reference standard +</th> <th>Reference standard -</th> <th>Total</th> <th rowspan="2">Raw data reported insufficiently meaning</th> </tr> </thead> <tbody> <tr> <td>Index test +</td> <td>7</td> <td>NR</td> <td>NR</td> </tr> </tbody> </table>						Reference standard +	Reference standard -	Total	Raw data reported insufficiently meaning specificity could not be calculated and is not reported	Index test +	7	NR	NR	Index test -	8	NR	NR	Total	15	NR	NR		Reference standard +	Reference standard -	Total	Raw data reported insufficiently meaning	Index test +	7	NR	NR
	Reference standard +	Reference standard -	Total	Raw data reported insufficiently meaning specificity could not be calculated and is not reported																											
Index test +	7	NR	NR																												
Index test -	8	NR	NR																												
Total	15	NR	NR																												
	Reference standard +	Reference standard -	Total	Raw data reported insufficiently meaning																											
Index test +	7	NR	NR																												

Reference	Bailitz 2009 ³				
	Index test –	12	NR	NR	specificity could not be calculated and is not reported
	Total	19	NR	NR	
	Clinically significant cervical spine injury – X-ray as index test (low risk)				
		Reference standard +	Reference standard –	Total	Raw data reported insufficiently meaning specificity could not be calculated and is not reported
	Index test +	4	NR	NR	
	Index test –	12	NR	NR	
	Total	16	NR	NR	
	Clinically significant cervical spine injury – CT as index test (high risk)				
		Reference standard +	Reference standard –	Total	Raw data reported insufficiently meaning specificity could not be calculated and is not reported
	Index test +	15	NR	NR	
	Index test –	0	NR	NR	
	Total	15	NR	NR	
	Clinically significant cervical spine injury – CT as index test (moderate risk)				
		Reference standard +	Reference standard –	Total	Raw data reported insufficiently meaning

Reference	Bailitz 2009 ³					
	Index test +	19	NR	NR	specificity could not be calculated and is not reported	
	Index test -	0	NR	NR		
	Total	19	NR	NR		
	Clinically significant cervical spine injury – CT as index test (low risk)					
		Reference standard +	Reference standard -	Total	Raw data reported insufficiently meaning specificity could not be calculated and is not reported	
	Index test +	16	NR	NR		
	Index test -	0	NR	NR		
	Total	16	R	NR		
	Statistical measures	<p>Clinically significant cervical spine injury – X-ray as index test (high risk): reported in paper</p> <p>Sensitivity: 46.0%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p> <p>Clinically significant cervical spine injury – X-ray as index test (moderate risk): reported in paper</p> <p>Sensitivity: 37.0%</p>				

Reference	Bailitz 2009³
	<p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p> <p>Clinically significant cervical spine injury – X-ray as index test (low risk): reported in paper</p> <p>Sensitivity: 25.0%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p> <p>Clinically significant cervical spine injury – CT as index test (same for high, moderate and low risk as all injuries detected): reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p>
Source of funding	Not reported
Limitations	Risk of bias: very serious – unclear if reference standard interpreted without knowledge of index test, unclear interval between index test and reference standard and unclear if reference standard contained the same components for all patients – applies to both index tests

Reference	Bailitz 2009³
	Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard included a 2 week follow-up period
Comments	None

Reference	Berne 1999⁴
Study type	Prospective study
Study methodology	Data source: study performed at level 1 academic urban trauma centre Recruitment: performed over an 8 month period (November 1996 to June 1997).
Number of patients	n = 58 (n=67 met inclusion criteria but n=9 were excluded as they did not get both plain radiography/X-ray and CT of the cervical spine, leaving n=58 analysed)
Patient characteristics	Age, mean (range): 43.1 (17-87) years Gender (male to female ratio): not reported Ethnicity: not reported Head injury: 53% had associated head injury (intracranial bleed), unclear if remaining suffered some form of head injury as part of the injury mechanism

Reference	Berne 1999 ⁴
	<p data-bbox="546 288 819 320">Mechanism of injury:</p> <ul data-bbox="595 347 999 595" style="list-style-type: none"><li data-bbox="595 347 999 379">• Motor vehicle crash, 36.2%<li data-bbox="595 384 999 416">• Fall from a height, 24.1%<li data-bbox="595 421 999 453">• Auto vs. pedestrian, 27.6%<li data-bbox="595 458 999 489">• Auto vs. bicycle, 3.4%<li data-bbox="595 494 999 526">• Motorcycle crash, 3.4%<li data-bbox="595 531 999 563">• Assault, 3.4%<li data-bbox="595 568 999 600">• Hanging, 1.7% <p data-bbox="546 679 1160 711">Injury severity score, mean (range): 24.1 (4-66)</p> <p data-bbox="546 796 685 828">Intubation:</p> <ul data-bbox="595 855 864 927" style="list-style-type: none"><li data-bbox="595 855 864 887">• In the field, 8.6%<li data-bbox="595 892 864 924">• In ED, 74.1% <p data-bbox="546 1008 801 1040">Associated injuries:</p> <ul data-bbox="595 1067 1066 1315" style="list-style-type: none"><li data-bbox="595 1067 1066 1099">• Head (intracranial bleed), 53.4%<li data-bbox="595 1104 1066 1136">• Thoracic, 29.3%<li data-bbox="595 1141 1066 1173">• Abdominal, 15.5%<li data-bbox="595 1177 1066 1209">• Pelvic fracture, 5.2%<li data-bbox="595 1214 1066 1246">• Spinal injury, 8.6%<li data-bbox="595 1251 1066 1283">• Upper extremity, 6.9%<li data-bbox="595 1287 1066 1319">• Lower extremity, 10.3%

Reference	<p>Berne 1999⁴</p> <p>Setting: secondary care – trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: high-risk blunt trauma; inability to evaluate patient’s cervical spine clinically due to head injury, shock, alcohol or illicit drug use or pharmacological sedation and/or paralysis; need for CT scan of another body areas besides the cervical spine; and need for intensive care unit admission.</p> <p>Exclusion criteria: haemodynamic instability preventing transportation to CT suite; pregnancy; age <17 years; and/or identification of a surgical emergency while scanning another area (for example, mass lesion on head CT scan).</p> <p>High risk blunt trauma with suspected cervical spine injury</p>
Target condition(s)	<p>Suspected cervical spine injury – 53% had associated head injury (intracranial bleed), unclear if remaining suffered some form of head injury as part of the injury mechanism (assumed head injury based on severity of injuries – all admitted to ICU/at high risk)</p>
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine (data not included further in review as not relevant as initial imaging in severely injured)</p> <p>CT of cervical spine</p>

Reference	Berne 1999⁴
	<p>Complete cervical helical CT scan including all seven cervical vertebrae and first thoracic vertebrae performed when patient sent to CT suite to evaluate other body areas. Data on associated injuries, time from admission to CT scan, type and effects of adverse events occurring in CT scanner and CT readings by attending radiologist blinded to cases collected.</p> <p><u>Reference standard</u></p> <p>Final diagnosis based on all imaging/studies, including plain radiography even when CT used as index test, unclear duration of follow-up. Initially underwent plain radiography (X-ray) followed by complete cervical helical CT scan. May include clinical examination findings for some.</p> <p>Radiological study considered positive if diagnostic or suspicious for cervical spine injury. True positive defined if attending radiologist considered study to be diagnostic for injury or when confirmed by complementary imaging (CT or plain radiography) for suspicious films. If complementary CT or plain radiography did not confirm suspicious studies an additional radiological study (MRI or flexion-extension films) or subsequent clinical examination where appropriate (recovery of normal sensorium) was used to correlate initial radiological findings. False positives were those where initial films were suspicious but not diagnosed by complementary radiological studies or clinical examination. A study was negative where no cervical spine injury was identified. True negatives were those where all radiological studies performed failed to reveal an abnormality suspicious for injury. False negative was when a complementary study in same patient revealed a previously unrecognised abnormality that was diagnostic for cervical spine injury.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index tests and subsequent tests/final confirmed diagnosis</p>
Outcome	<p>Any cervical spine injury (stable and unstable)</p> <p>and</p>

Reference	Berne 1999 ⁴				
	Unstable cervical spine injury – classified as unstable in consultation with combined neurosurgical-orthopaedic spine service and based on published guidelines				
2x2 table	Any cervical spine injury – X-ray as index test				
		Reference standard +	Reference standard –	Total	
	Index test +	12	0	12	
	Index test –	8	38	46	
	Total	20	38	58	
	Any cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	
	Index test +	18	0	18	
	Index test –	2	38	40	
	Total	20	38	58	
	Unstable cervical spine injury – X-ray as index test				
		Reference standard +	Reference standard –	Total	Raw data not provided so calculated using excel sheet

Reference	Berne 1999 ⁴					
	Index test +	5	0	5	from sensitivity/specificity etc. reported in the paper	
	Index test –	3	50	53		
	Total	8	50	58		
	Unstable cervical spine injury – CT as index test					
		Reference standard +	Reference standard –	Total	Raw data not provided so calculated using excel sheet from sensitivity/specificity etc. reported in the paper	
	Index test +	8	0	8		
	Index test –	0	50	50		
	Total	8	50	58		
	Statistical measures	<p>Any cervical spine injury – X-ray as index test: reported in paper</p> <p>Sensitivity: 60.0%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 82.6%</p> <p>Any cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 90.0%</p>				

Reference	Berne 1999⁴
	<p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 95.0%</p> <p>Unstable cervical spine injury – X-ray as index test: reported in paper</p> <p>Sensitivity: 62.5%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 92.7%</p> <p>Unstable cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 100.0%</p>
Source of funding	Not reported
Limitations	Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test, unclear time interval between index test and reference standard and likely that reference standard components differed between patients – applies to both index tests

Reference	Berne 1999⁴
	Indirectness: very serious – all included were at high-risk/admitted to ICU representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and unclear if reference standard included a 2 week follow-up period
Comments	None

Reference	Brohi 2005⁶
Study type	Retrospective
Study methodology	Data source: people undergoing new spinal assessment protocol from single hospital Recruitment: new protocol introduced in February 2002 and patients included in the study between then and January 2004.
Number of patients	n = 421 analysed for X-ray and n=381 analysed for CT (n=442 considered relevant to review population; for X-ray, those without both CT and X-ray of cervical spine were excluded, leaving n=421; for CT, those without both CT and clinical outcome/MRI were excluded, leaving n=381)
Patient characteristics	Age, median (IQR): 34 (25-50) years Gender (male to female ratio): 2.6:1 Ethnicity: not reported Head injury: unclear if all or most had head injury as no details provided Setting: secondary care – intubated trauma patients in hospital Country: UK

Reference	Brohi 2005 ⁶
	<p>Inclusion criteria: unconscious, intubated trauma patients</p> <p>Exclusion criteria: not reported</p> <p>Unconscious, intubated patients with suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided (assumed head injury based on severity of injuries – all unconscious and intubated)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine (data not included further in review as not relevant as initial imaging in severely injured)</p> <p>CT of cervical spine</p> <p>Single-slice helical CT performed from base of skull to first thoracic vertebra. Performed at 2 mm thickness and 1.5 mm pitch with sagittal and coronal reformations.</p> <p><u>Reference standard</u></p> <p>Final diagnosis, including all imaging performed (MRI in some) and follow-up through hospital stay to identify missed injuries</p> <p>MRI was performed if CT scan or lateral radiograph suggested ligamentous injury or instability, if there were neurological signs of spinal cord injury before intubation or if there were contradictory findings between plain film and CT imaging. Consultant trauma radiologist (board-certified or equivalent) reported the images. If all imaging</p>

Reference	Brohi 2005⁶				
	was normal, spine was cleared and spinal precautions removed. Patients assessed once they regained consciousness and followed through their hospital stay for any evidence of missed spinal injury.				
	Time between measurement of index test and reference standard: unclear duration between index tests and other imaging/final diagnosis being confirmed				
Outcome	Any cervical spine injury				
	and				
	Unstable cervical spine injury – defined using White and Punjabi system and three-column model of Denis				
2x2 table	Any cervical spine injury – X-ray as index test				
		Reference standard +	Reference standard –	Total	Results for ‘all laterals’ reported including all films rather than just those deemed ‘adequate’.
	Index test +	44	21	65	
	Index test –	17	339	356	
	Total	61	360	421	
	Any cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	
	Index test +	51	4	55	

Reference	Brohi 2005 ⁶				
	Index test –	1	325	326	
	Total	52	329	381	
	Unstable cervical spine injury – X-ray as index test				
		Reference standard +	Reference standard –	Total	Results only available for the subgroup that had ‘adequate’ films, which was n=200.
	Index test +	24	14	38	
	Index test –	8	154	162	
	Total	31	168	200	
	Unstable cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	
	Index test +	29	4	33	
	Index test –	0	348	348	
	Total	29	352	381	
	Statistical measures	Any cervical spine injury – X-ray as index test: reported in paper (apart from PPV which was calculated using excel) Sensitivity: 72.1%			

Reference	Brohi 2005 ⁶
	<p data-bbox="546 229 779 256">Specificity: 94.2%</p> <p data-bbox="546 288 707 316">PPV: 68.0%</p> <p data-bbox="546 347 707 375">NPV: 95.2%</p> <p data-bbox="546 464 1973 523">Any cervical spine injury – CT as index test: reported in paper (apart from PPV which was calculated using excel)</p> <p data-bbox="546 555 779 582">Sensitivity: 98.1%</p> <p data-bbox="546 614 779 641">Specificity: 98.8%</p> <p data-bbox="546 673 707 700">PPV: 93.0%</p> <p data-bbox="546 732 707 759">NPV: 99.7%</p> <p data-bbox="546 849 1995 908">Unstable cervical spine injury – X-ray as index test: reported in paper (apart from PPV which was calculated using excel)</p> <p data-bbox="546 940 779 967">Sensitivity: 75.0%</p> <p data-bbox="546 999 779 1026">Specificity: 91.7%</p> <p data-bbox="546 1058 707 1085">PPV: 63.0%</p> <p data-bbox="546 1117 707 1144">NPV: 95.1%</p> <p data-bbox="546 1233 1962 1292">Unstable cervical spine injury – CT as index test: reported in paper (apart from PPV which was calculated using excel)</p>

Reference	Brohi 2005⁶
	<p>Sensitivity: 100.0%</p> <p>Specificity: 99.0%</p> <p>PPV: 88.0%</p> <p>NPV: 100.0%</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if index test and reference standard interpreted without knowledge of the other, unclear time interval between index test and reference standard and likely that reference standard components differed between patients – applies to both index tests</p> <p>Indirectness: very serious – all included were at unconscious and intubated representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and unclear if reference standard included a 2 week follow-up period</p>
Comments	None

Reference	Bush 2016⁷
Study type	Prospective study
Study methodology	<p>Data source: Conducted at an American College of Surgeons-verified Level 1 trauma centre.</p> <p>Recruitment: conducted between March 2014 and March 2015.</p>

Reference	Bush 2016 ⁷
Number of patients	<p>n = 1668 (only provides useable results for the n=632 that were intoxicated by alcohol and/or drugs)</p> <p>(n=1696 underwent cervical spine CT with n=28 of these subsequently excluded from the overall population for unclear reasons; useable results were only provided for n=632 in intoxicated subgroup)</p>
Patient characteristics	<p>Age, mean (SD): 45 (17), 39 (14) and 43 (17) in subgroups intoxicated by alcohol only, drugs only or alcohol and drugs</p> <p>Gender (male to female ratio): 71.7% male and 28.3% female</p> <p>Ethnicity: not reported</p> <p>Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p>Mechanism of injury – reported for whole population as breakdown not given specifically for the intoxicated group</p> <ul style="list-style-type: none"> • Motor vehicle crash, 28.2% • Ground-level fall, 20.2% • Other mechanism, 15.8% • Fall from height, 14.5% • Motorcycle crash, 6.9% • Automobile vs. pedestrian, 5.5%

Reference	Bush 2016 ⁷
	<ul style="list-style-type: none">• Assault, 5.5%• Bicycle vs. automobile, 3.4% <p>GCS score:</p> <ul style="list-style-type: none">• GCS score 15, 52.8%• GCS score 9-14, 33.7%• GCS score <9, 13.4% <p>Injury Severity Score, mean (range): 8 (8), 12 (10) and 9 (10) in subgroups intoxicated by alcohol only, drugs only or alcohol and drugs</p> <p>Additional imaging, 85 (5%) – reported for whole population as breakdown not given specifically for the intoxicated group</p> <p>Setting: secondary care – trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: adults (≥18 years) with blunt trauma; and underwent evaluation of cervical spine with cervical CT scan – only provides results for the group of participants that were intoxicated (defined as a blood alcohol</p>

Reference	Bush 2016⁷
	<p>level greater than 80 mg/dL and/or a positive urine drug screen that was not attributable to field or emergency department medication administration).</p> <p>Exclusion criteria: patients presenting in a delayed manner after the index trauma, transfer patients without available CT images from the referring facility who did not undergo repeated CT scans at our facility, and patients with known recent cervical spine fractures or surgery</p> <p>Adults with suspected cervical spine injury undergoing CT (results only provided for those that were intoxicated)</p>
Target condition(s)	Suspected cervical spine injury in those that were intoxicated – unclear if most/all had head injury
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>CT scans performed using one of two emergency department imagers. CT protocol included continuous image acquisition from the skull base through the T1 vertebral body using 2-mm slice thickness. Axial images as well as coronal and sagittal reconstructions were immediately reviewed and interpreted one of eight certified radiologists, two of whom were neuroradiologists.</p> <p><u>Reference standard</u></p> <p>Cervical spine injury diagnosis at discharge/follow-up – includes composite end-point, which included MRI findings, operative findings and clinical status at discharge. Likely to differ between patients as not all would have had MRI and same imaging during stay. Also mentions identification of missed clinically significant injuries from outpatient notes following discharge. Unclear how long this followup was for and whether the same in all patients.</p>

Reference	Bush 2016⁷				
	All patients followed up through completion of hospital stay and re-evaluated at time of discharge, which included recording of any interval diagnosis of cervical spine pathology as well as other details.				
	Time between measurement of index test and reference standard: unclear, varies between patients as components of additional imaging/follow-up prior to discharge and following discharge likely differ				
Outcome	Cervical spine injury – any bony, ligamentous or spinal cord injury.				
	Unstable cervical spine injury – any injury that required or benefitted from spine immobilisation or alternatively was at risk of any adverse effect because of the removal of spine precautions. Any injury defined as unstable or potentially unstable injury that required surgical stabilisation or prolonged immobilisation.				
2x2 table	All cervical spine injuries – CT vs. reference standard				
		Reference standard +	Reference standard –	Total	Note: results only given for the subgroup that were intoxicated. Raw data calculated from diagnostic accuracy measures provided in paper.
	Index test +	56	1	57	
	Index test –	5	570	575	
	Total	61	571	632	
	Unstable cervical spine injuries – CT vs. reference standard				
		Reference standard +	Reference standard –	Total	Note: results only given for the subgroup that were intoxicated.
	Index test +	13	0	13	

Reference	Bush 2016 ⁷				
	Index test –	1	617	618	Raw data calculated from diagnostic accuracy measures provided in paper – does not quite total 632 which is the number said to be analysed.
	Total	14	617	631	
Statistical measures	<p>All cervical spine injuries – CT vs. references standard (intoxicated patients) – reported in the paper</p> <p>Sensitivity: 92.9%</p> <p>Specificity: 99.8%</p> <p>PPV: 98.5%</p> <p>NPV: 99.2%</p> <p>Unstable cervical spine injuries – CT vs. reference standard (intoxicated patients) – reported in the paper</p> <p>Sensitivity: 91.6%</p> <p>Specificity: 100%</p> <p>PPV: 100%</p> <p>NPV: 99.8%</p>				
Source of funding	Not reported				
Limitations	Risk of bias: very serious – unclear if consecutive sample enrolled and reasons for exclusion not reported, some concerns about whether the reference standard was interpreted without knowledge of the index test, unclear follow-up time period for assessing reference standard outcome and references standard components likely differed between participants				

Reference	Bush 2016⁷
	Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, also limited to very specific population of those that were intoxicated and unclear time-point for reference standard and whether it matches protocol
Comments	2x2 data not reported so calculated from the diagnostic accuracy measures reported (sensitivity etc.)

Reference	Cohn 1991⁹
Study type	Prospective study
Study methodology	Data source: data from a single university medical centre Recruitment: between July 1989 and August 1989, consecutive patients admitted with blunt traumatic injury were evaluated for cervical spine injury
Number of patients	n = 60 (n=60 said to be evaluated and n=60 analysed)
Patient characteristics	Age, mean (SD): not reported Gender (male to female ratio): not reported Ethnicity: not reported

Reference	Cohn 1991 ⁹
	<p data-bbox="546 229 1984 293">Head injury: 50% had head CT as part of diagnostic tests, unclear if remaining patients had some form of head injury as part of the injury mechanism</p> <p data-bbox="546 379 792 408">Altered sensorium:</p> <ul data-bbox="595 440 1034 542" style="list-style-type: none"><li data-bbox="595 440 945 469">• GCS score <15, 48.3%<li data-bbox="595 475 1034 504">• Coma (GCS score <8), 15.0%<li data-bbox="595 510 887 539">• Intoxicated, 35.0% <p data-bbox="546 628 922 657">Abnormal neck exam, 11.7%</p> <p data-bbox="546 743 775 772">Cord injury, 1.7%</p> <p data-bbox="546 858 837 887">Shock (BP <80), 3.3%</p> <p data-bbox="546 973 1460 1002">Setting: secondary care – admitted to centre with blunt traumatic injury</p> <p data-bbox="546 1088 730 1117">Country: USA</p> <p data-bbox="546 1203 1648 1232">Inclusion criteria: blunt traumatic injury evaluated for presence of cervical spine injury</p>

Reference	Cohn 1991⁹
	Exclusion criteria: not reported
	People with blunt traumatic injury admitted to centre, with suspected cervical spine injury
Target condition(s)	Suspected cervical spine injury – 50% had head CT as part of diagnostic tests, unclear if remaining patients had some form of head injury as part of the injury mechanism
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p>Performed in the trauma room after sensorium and neck assessment/examination. Initially evaluated by radiology resident and trauma chief resident for presence of pathology. Completion cervical spine studies included more sophisticated studies (wide supra) when needed to exclude injury. All patients managed in cervical collars until cleared of spine injury.</p> <p><u>Reference standard</u></p> <p>Reference standard unclear, possibly a final diagnosis based on any further imaging performed (including flexion/extension views, cervical CT scans or tomograms where indicated)</p> <p>Time between measurement of index test and reference standard: unclear time interval between index tests and subsequent tests/final confirmed diagnosis</p>
Outcome	Acute cervical spine injuries – poorly defined
2x2 table	Acute cervical spine injury – X-ray as index test

Reference	Cohn 1991 ⁹				
		Reference standard +	Reference standard -	Total	Data reported insufficiently meaning specificity could not be calculated and it was not reported in the paper.
	Index test +	4	NR	NR	
	Index test -	3	NR	NR	
	Total	7	53	60	
Statistical measures	<p>Acute cervical spine injury – X-ray as index test: calculated using excel sheet</p> <p>Sensitivity: 57.0%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p>				
Source of funding	Not reported				
Limitations	<p>Risk of bias: very serious – unclear if reference standard interpreted without knowledge of index test, unclear interval between index test and reference standard and unclear if reference standard contained the same components for all patients</p> <p>Indirectness: very serious – head CT performed for 50% but unclear if remaining also had head injury as part of injury mechanism, and unclear if reference standard included a 2 week follow-up period</p>				
Comments	None				

Reference	Dan Lantsman 2020¹⁰
Study type	Retrospective cohort study
Study methodology	Data source: review of records of those admitted to emergency room. Picture computerised archive system (PACS) used to extract whole spine CT examinations. Recruitment: review of medical records and whole spine CT scans performed between 2017 and 2018
Number of patients	n = 147 (n=129 analysed, as n=9 were excluded due to poor X-ray quality and n=9 were excluded due to missing radiographs)
Patient characteristics	Characteristics are provided for the n=147 included in the study initially, not the n=129 analysed as part of the diagnostic accuracy assessment Age, median (IQR): 83 (77-88) years Gender (male to female ratio): 43.5% male and 56.5% female Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: not reported

Reference	Dan Lantsman 2020¹⁰
	<p>Setting: secondary care – emergency room following low-energy trauma</p> <p>Country: Israel</p> <p>Inclusion criteria: radiographic diagnosis of diffuse idiopathic skeletal hyperostosis (DISH); following low-energy trauma (traumatic or accidental injury with a maximal Injury Severity Score of 9/75 not requiring invasive procedures); and underwent a whole spine CT with radiographs for at least the thoracic and lumbar spine.</p> <p>Exclusion criteria: spinal CT examination did not confirm DISH; those with known malignant spinal involvement or ankylosing spondylitis; those with missing spinal radiographs (except for if they were missing only cervical spine radiographs); and with poor radiography quality</p> <p>Those with suspected spine injury with DISH following low-energy trauma (separate results for cervical spine injuries)</p>
Target condition(s)	Suspected spine injury in those with DISH following low-energy trauma – spine in general but provides results separately for cervical spine region – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray (radiographs) – performed in anterior-posterior and lateral projections.</p> <p><u>Reference standard</u></p> <p>Whole spine CT scan – performed in axial plane on 64-Slice machine. Images reconstructed in bone and soft tissue algorithms and reformatted in sagittal and coronal planes.</p>

Reference	Dan Lantsman 2020¹⁰
	<p>Spinal radiographs and whole spine CT were evaluated separately for presence of spinal fractures by a single reader (third year radiology resident) with at least 1-month interval between readings. Reader was blinded to patient clinical data (apart from age and gender) and the radiographic report. Fractures and locations recorded for radiographs and CT scans and classified as acute or chronic fractures. Acute fractures were those not present in previous studies and consisting of a radiographically depicted cortical disruption or impaction of the trabeculae and paravertebral soft tissue infiltration. Chronic fractures were those detected and unchanged from previous radiological studies and consisting of any degree of remodelling and smoothing of cortical edges with no anterior vertebral body buckling. Second reading by a senior, experienced musculoskeletal radiology was performed on 10% of radiographs and CT scans.</p> <p>Time between measurement of index test and reference standard: describes at least 1 month interval between readings – unclear if this is between multiple readings of the same imaging (e.g. X-ray and a subsequent X-ray), or between X-ray and reference standard (CT).</p>
Outcome	Acute fracture - those not present in previous studies and consisting of a radiographically depicted cortical disruption or impaction of the trabeculae and paravertebral soft tissue infiltration.
2x2 table	2x2 tables could not be reported as raw data not reported for cervical spine injuries specifically. Attempted to calculate raw data from diagnostic accuracy measures reported in the paper but not possible given 0 values for sensitivity and PPV.
Statistical measures	<p>X-ray vs. reference standard (whole spine CT) – reported in paper</p> <p>Sensitivity: 0%</p> <p>Specificity: 100%</p> <p>PPV: 0%</p> <p>NPV: 96.9%</p>

Reference	Dan Lantsman 2020¹⁰
Source of funding	Reported to be no funding for the study.
Limitations	<p>Risk of bias: serious – unclear if consecutive sample enrolled, not all were analysed as some were missing radiographs or had poor quality radiographs and unclear duration between index test and reference standard</p> <p>Indirectness: very serious - head injury not mentioned and unclear if all or most had head injury. Very specific population of those with DISH, a condition making injuries more likely following lower impact trauma. Also, injury reported was specifically fracture not any type of injury.</p>
Comments	2x2 tables could not be reported as raw data not reported for cervical spine injuries specifically. Attempted to calculate raw data from diagnostic accuracy measures reported in the paper but not possible given 0 values for sensitivity and PPV.

Reference	Duane 2008¹⁴
Study type	Prospective
Study methodology	<p>Data source: evaluation of those admitted to a single level 1 trauma centre</p> <p>Recruitment: prospective evaluation between February 2004 and September 2006 of all blunt trauma team alert patients >16 years admitted to single level 1 trauma centre</p>
Number of patients	<p>n = 1004</p> <p>(N=4608 patients >16 years with blunt trauma identified, with n=1004 subsequently included and analysed as they had both lateral cervical spine films and CT of the cervical spine)</p>
Patient characteristics	<p><u>Note: n=84 in fracture group and n=920 in no fracture group</u></p> <p>Age, mean (SD): 41.3 (19.0) years in fracture group and 41.3 (21.0) years in no fracture group</p>

Reference	Duane 2008 ¹⁴
	<p data-bbox="548 229 1805 261">Gender (male to female ratio): 61.9% male in fracture group and 64.3% male in no fracture group</p> <p data-bbox="548 347 1543 379">Ethnicity: 62.0% white in fracture group and 59.0% white in no fracture group</p> <p data-bbox="548 466 1747 497">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="548 584 1946 647">Mechanism of injury: 72.6% in fracture group and 77.4% in no fracture group had injury due to motor vehicle collision.</p> <p data-bbox="548 730 1818 762">GCS score at initial trauma, mean (SD): 12.4 (4.6) vs. 14.0 (3.0) in fracture and no fracture groups</p> <p data-bbox="548 849 1771 880">Injury Severity Score, mean (SD): 20.8 (14.2) vs. 11.6 (10.6) in fracture and no fracture groups</p> <p data-bbox="548 967 1070 999">Setting: secondary care – trauma centre</p> <p data-bbox="548 1085 730 1117">Country: USA</p> <p data-bbox="548 1203 1926 1267">Inclusion criteria: blunt trauma team alert patients; >16 years; admitted to single level 1 trauma centre; and underwent both lateral cervical spine film and cervical spine CT</p>

Reference	Duane 2008¹⁴			
	Exclusion criteria: not reported			
	People admitted to trauma centre with blunt injury and suspected cervical spine injury			
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided			
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p><u>Reference standard</u></p> <p>CT of cervical spine – gold standard for fractures</p> <p>CT of cervical spine used as gold standard for diagnosis of cervical spine fracture. At time of study, standard approach for all trauma activation patients was thorough clinical examination followed by cervical spine film. All patients, regardless of level of consciousness or intoxication then had CT of cervical spine. Further radiographic studies then performed based on results of initial CT scan.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and reference standard</p>			
Outcome	Cervical spine fracture			
2x2 table	Cervical spine fracture – X-ray as index test			
		Reference standard +	Reference standard –	Total
Index test +		16	7	23

Reference	Duane 2008¹⁴			
	Index test –	68	913	981
	Total	84	920	1004
Statistical measures	<p>Cervical spine fracture – X-ray as index test: reported in paper</p> <p>Sensitivity: 19.0%</p> <p>Specificity: 99.2%</p> <p>PPV: 69.6%</p> <p>NPV: 93.1%</p>			
Source of funding	Not reported			
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test and unclear time interval between index test</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and outcome limited to fractures rather than any cervical spine injury</p>			
Comments	None			

Reference	Duane 2010¹³
Study type	Retrospective
Study methodology	Data source: retrospective review of established trauma registry and chart review

Reference	Duane 2010¹³
	Recruitment: retrospectively matching inclusion criteria between January 2000 and December 2008 from single level 1 trauma centre
Number of patients	n = 49 (n=271 matching inclusion criteria that underwent flexion-extension films, with n=49 eventually included as they also had MRI of the cervical spine)
Patient characteristics	<p>Age, mean (SD): 37.9 (17.7) years</p> <p>Gender (male to female ratio): 69.4% males</p> <p>Ethnicity: 49.0% white</p> <p>Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p>Mechanism of injury:</p> <ul style="list-style-type: none"> • Motor vehicle collision, 69.0% • Falls, 16.0% • Other, 15.0% <p>GCS score, mean (SD): 13.8 (3.5)</p>

Reference	Duane 2010¹³
	<p>Injury Severity Score, mean (SD): 15.6 (10.2)</p> <p>Duration of stay, mean (SD): 8.0 (11.2) days</p> <p>Initial lactate: 2.2 (1.7) mmol/L</p> <p>Setting: secondary care – data from trauma registry</p> <p>Country: USA</p> <p>Inclusion criteria: adults (≥18 years) sustaining blunt trauma; and had flexion-extension plain films and subsequent MRI evaluation of cervical spine.</p> <p>Exclusion criteria: not reported</p> <p>Adults with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p>

Reference	Duane 2010¹³				
	<p><u>Reference standard</u></p> <p>MRI – gold standard for ligamentous injuries</p> <p>Flexion-extension considered complete if it visualised from the first cervical spine through to the bottom of the first thoracic spine and >30° excursion on both flexion and extension. All performed actively without fluoroscopy. Flexion-extension compared with MRI as the gold standard for diagnosis of ligamentous injury. MRI performed using Siemens Avanto 1.5T with scans performed without contrast. Multiple sequences included: T1 turbo spin echo (TSE) sagittal, T2 TSE sagittal, T2 short tau inversion recovery sagittal, T2* multiple echo data image combination or gradient echo axial, T2 TSE axial and fast low-angle shot two-dimensional sagittal gradient echo.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and reference standard</p>				
Outcome	Ligamentous injury of the cervical spine				
2x2 table	Ligamentous cervical spine injury – X-ray as index test				
		Reference standard +	Reference standard –	Total	Of the 8 ligamentous injuries missed by X-ray, five were significant (n=2 associated fractures requiring prolonged collar and n=3 operative intervention)
Index test +	0	1	1	1	
Index test –	8	40	48	48	
Total	8	41	49	49	
Statistical measures	Ligamentous cervical spine injury – X-ray as index test: reported in paper				

Reference	Duane 2010¹³
	<p>Sensitivity: 0.0%</p> <p>Specificity: 98.0%</p> <p>PPV: 0.0%</p> <p>NPV: 83.0%</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test and unclear time interval between index test</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and outcome limited to ligamentous injuries rather than any cervical spine injury</p>
Comments	None

Reference	Duane 2016¹⁶
Study type	Retrospective study
Study methodology	<p>Data source: retrospective review of trauma registry</p> <p>Recruitment: those presenting as blunt trauma team alert patients between January 2008 and May 2014 at American College of Surgeons verified level I trauma centre (Virginia Commonwealth University Medical Center)</p>
Number of patients	<p>n = 9227</p> <p>(patient flow not well described)</p>

Reference	Duane 2016 ¹⁶
Patient characteristics	<p>Age, mean (SD): 39.4 (17.5) years</p> <p>Gender (male to female ratio): 64.4% male and 35.6% female</p> <p>Ethnicity: not reported</p> <p>Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p>Mechanism of injury:</p> <ul style="list-style-type: none">• Motor vehicle collision, 59%• Falls, 12%• Motorcycle collision, 10%• Pedestrian struck, 10%• Other/unknown, 9% <p>GCS score, mean (SD; median): 14.3 (2.4; 15)</p> <p>Setting: secondary care – trauma centre</p>

Reference	Duane 2016¹⁶
	<p>Country: USA</p> <p>Inclusion criteria: adults (≥18 years) with blunt trauma; and underwent screening CT to diagnose or rule-out cervical spine injury.</p> <p>Exclusion criteria: none reported</p> <p>Adults following trauma undergoing assessment of cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT scan</p> <p>Using 64-multidetector CT between 2008 and 2011 and a 128-multidetector CT between 2011 and 2014. 2-mm thick axial cuts performed at 2-mm increments with multiplanar reformatted images.</p> <p><u>Reference standard</u></p> <p>Later found to have cervical spine injury – poorly described. Likely involves any other findings during follow-up but duration of follow-up available unclear. CT considered the standard for presence or absence of fracture and magnetic resonance imaging for ligament injury. MRI performed in some as indicated but not all patients. For MIR, 3-mm sagittal and axial cuts with 0.3 mm standard of error.</p>

Reference	Duane 2016¹⁶			
	<p>Haemodynamically stable patients were evaluated by non-contrast CT of cervical spine. Those that were unstable had their cervical collar maintained and spine examination and CT deferred until patient had stabilised. Post-CT management was as follows: normal CT result and conscious had cervical spine re-evaluated for midline tenderness. If no tenderness then collar was removed. If tenderness present then collar was maintained for 2 weeks and examination repeated. If significant tenderness persisted then an MRI was obtained. If normal, collar was removed and physical therapy started. If there was an abnormal result, management was based on specialist consultation. Patients with a normal CT who could not participate in their own evaluation (GCS score <15) underwent MRI and further management as above. For those with an abnormal CT result, liberal use of MRI and spine consultations was used.</p> <p>For all imaging, only final attending radiologist reads of scans were considered. Negative CT or MRI results were defined as high quality images without motion artifacts with no fracture and/or ligament injury identified. Positive CT or MRI defined as one where a fracture or ligament injury was identified or could not be excluded. Specific findings suggestive of ligamentous injury included abnormal vertebral alignment, increased space between ligamentous columns or other contiguous structures and prevertebral haematoma or oedema.</p> <p>Time between measurement of index test and reference standard: unclear, likely that reference standard components and timeinterval differs between patients.</p>			
Outcome	<p>Fracture and/or ligamentous injury</p> <p>Ligamentous injury - specific findings suggestive of ligamentous injury included abnormal vertebral alignment, increased space between ligamentous columns or other contiguous structures and prevertebral haematoma or oedema.</p>			
2x2 table	CT vs. reference standard (later diagnosis of injury) – fracture and/or ligamentous injury			
		Reference standard +	Reference standard –	Total

Reference	Duane 2016 ¹⁶				
	Index test +	561	6	567	Raw data calculated from diagnostic accuracy measures provided in paper.
	Index test -	0	8660	8660	
	Total	561	8666	9227	
	Note: number of true positives does not match that reported in paper (n=553) but insufficient data provided to calculate diagnostic accuracy results from raw data.				
	CT vs. reference standard (later diagnosis of injury) – ligamentous injury (with or without an associated fracture)				
		Reference standard +	Reference standard -	Total	Raw data calculated from diagnostic accuracy measures provided in paper.
	Index test +	29	9	38	
	Index test -	28	9160	9188	
	Total	57	9169	9226	Note: total number calculated from diagnostic accuracy measures reported does not quite match 9227 reported in the paper.
	Note: all ligamentous injuries were also associated with a fracture so no individuals with a ligamentous injury were				

Reference	Duane 2016¹⁶
	missed by CT, as they had a fracture that was picked up by CT.
Statistical measures	<p>CT vs. reference standard (later diagnosis of injury) – fracture and/or ligamentous injury – reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 99.93%</p> <p>PPV: 98.93%</p> <p>NPV: 100%</p> <p>CT vs. reference standard (later diagnosis of injury) – ligamentous injury (with or without an associated fracture) – reported in paper</p> <p>Sensitivity: 50.88%</p> <p>Specificity: 99.90%</p> <p>PPV: 76.31%</p> <p>NPV: 99.69%</p> <p>Note: all of these ligamentous injuries were also associated with a fracture, which were all picked up by CT</p>
Source of funding	Not reported
Limitations	Risk of bias: very serious –unclear if consecutive sample enrolled, reference standard poorly described and likely to have been interpreted with knowledge of index test, unclear time interval between index test and reference standard and likely that reference standard different between patients

Reference	Duane 2016¹⁶
	Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard matches protocol as poorly defined
Comments	2x2 data not reported so calculated from the diagnostic accuracy measures reported (sensitivity etc.)

Reference	Fisher 2013¹⁷
Study type	Retrospective study
Study methodology	Data source: subjects identified using trauma registry at University Medical Center, a level I academic trauma centre in Lubbock, Texas. Recruitment: included those matching inclusion criteria and admitted between 1 st January 2005 and 30 th March 2012.
Number of patients	n = 277(n=1354 blunt trauma patients admitted and n=277 subsequently included as they had both a CT and MRI performed of cervical spine)
Patient characteristics	Age, mean (range): 35.2 (0-93) years <ul style="list-style-type: none"> • Children <18 years, 14% Gender (male to female ratio): 70% males and 30% females Ethnicity: not reported

Reference	Fisher 2013 ¹⁷
	<p data-bbox="546 229 1749 261">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="546 347 819 379">Mechanism of injury:</p> <ul data-bbox="595 405 1039 676" style="list-style-type: none"><li data-bbox="595 405 1021 437">• Motor vehicle collisions, 70%<li data-bbox="595 469 763 501">• Falls, 9%<li data-bbox="595 533 797 564">• Assault, 8%<li data-bbox="595 596 1039 628">• Pedestrian/bike accidents, 3%<li data-bbox="595 660 792 692">• Other, 10% <p data-bbox="546 762 1003 794">GCS score, mean (range): 6 (3-14)</p> <p data-bbox="546 880 1151 912">Injury Severity Score, mean (range): 22 (0-75)</p> <p data-bbox="546 999 1178 1031">Duration of stay, mean (range): 15.3 (1-66) days</p> <p data-bbox="546 1117 1070 1149">Setting: secondary care – trauma centre</p> <p data-bbox="546 1235 730 1267">Country: USA</p>

Reference	Fisher 2013¹⁷
	<p>Inclusion criteria: blunt trauma patients with GCS score <15; and underwent both a CT scan and MRI of the cervical spine.</p> <p>Exclusion criteria: none reported</p> <p>People with blunt trauma and suspected cervical spine injury (majority adults at least 18 years old, 86%)</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided (assumed to have head injury based on severity of injuries – all obtunded)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT – performed with 64-slice or 16-slice scanner.</p> <p>OR</p> <p>MRI – performed using General Electric HDX scanner.</p> <p><u>Reference standard</u></p> <p>Diagnosis of clinically significant cervical spine injury by any modality – this was used in the study as the denominator as they noted a lack of an external gold standard. The use of this as the denominator does not allow specificity to be calculated.</p>

Reference	Fisher 2013¹⁷
	Time between measurement of index test and reference standard: MRI was obtained an average of 3.3 days (range 0-39) days after admission. Unclear whether this gives an indication of time between CT and MRI as unclear if CT performed immediately on admission for all.
Outcome	Clinically significant cervical spine injury CT and MRI scans considered clinically significant if detecting one of the following: ligamentous injury in two adjacent spinal columns, subluxations, cord injury, nerve root injury, disc herniations, and fractures except the following types as specified by NEXUS: spinous process fracture without involvement of the lamina, transverse process fracture without involvement of the facet joint, osteophyte fracture not including corner or teardrop fracture, isolated avulsion without associated ligamentous injury, simple wedge-compression fracture without loss of greater than or equal to 25% of vertebral body height, endplate fracture, type 1 odontoid fracture, and injury to the trabecular bone.
2x2 table	Raw data provided but difficult to understand – attempted calculations of true positives and false positives do not match sensitivity values reported in the paper for CT and MRI and therefore values reported in paper used and 2x2 tables not completed.
Statistical measures	<p>CT vs. reference standard (CT + MRI) for clinically significant cervical spine injuries</p> <p>Sensitivity: 83%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p> <p>MRI vs. reference standard (CT + MRI) for clinically significant cervical spine injuries</p> <p>Sensitivity: 89%</p> <p>Specificity: NR</p>

Reference	Fisher 2013¹⁷
	<p>PPV: NR</p> <p>NPV: NR</p> <p>Specificity could not be calculated as the combine CT + MRI was used as the reference standard, meaning it is not possible for there to be any false positives.</p> <p>N=70 were positive on both modalities (of these, n=1 clinically insignificant on CT but significant on MRI), n=11 were positive on CT but negative on MRI, n=150 were negative on both CT and MRI and n=12 were negative on CT but positive for clinically significant injury on MRI. An additional n=34 were negative on CT and positive on MRI, but with clinically insignificant injuries that did not form part of the calculation of sensitivity for clinically significant injuries.</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and mean time interval between index test and reference standard possibly at least 3 days – applies to both index tests</p> <p>Indirectness: serious – all included were obtunded representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p>
Comments	<p>Study notes the intention was not to compare the accuracy of CT and MRI as a solo modality but to assess the added value of MRI to more safely clear the cervical spine.</p> <p>Not possible to calculate specificity based on the reference standard used.</p>

Reference	Friesen 2014¹⁸
Study type	Retrospective
Study methodology	<p>Data source: retrospective search of radiology information system database containing radiological information from three major public emergency departments</p> <p>Recruitment: retrospective review of people matching inclusion criteria from database of three major public emergency departments between 12th January 2010 and 22nd June 2012 – another time-period mentioned but not relevant to review protocol</p>
Number of patients	<p>n = 206 undergoing both MRI and CT of cervical spine</p> <p>(n=783 identified as relevant to the study and n=206 subsequently included in analysis as they had both CT and MRI of cervical spine)</p>
Patient characteristics	<p><u>Note: characteristics only reported for whole group (n=783) and not the relevant group analysed (n=206)</u></p> <p>Age, mean (SD): 60 (25) years</p> <p>Gender (male to female ratio): 55.0% males</p> <p>Ethnicity: not reported</p> <p>Head injury: 76% with head CT as well as cervical spine CT</p> <p>Mechanism of injury: not reported</p>

Reference	Friesen 2014¹⁸
	<p>GCS score, mean (SD): not reported</p> <p>Injury Severity Score, mean (range): not reported</p> <p>Setting: secondary care – database of emergency department data</p> <p>Country: Australia</p> <p>Inclusion criteria: aged ≥ 16 years; and CT and MRI performed for suspected blunt acute cervical spine trauma between 12th January 2010 and 22nd June 2012</p> <p>Exclusion criteria: not reported</p> <p>Adults with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – 76% said to have had brain CT alongside cervical spine imaging, therefore not downgraded for indirectness
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p>

Reference	Friesen 2014¹⁸								
	<p><u>Reference standard</u></p> <p>MRI reported in paper to be reference standard, but not in line with this review protocol. Therefore, data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>Images from MRI and CT examinations retrospectively reviewed by consultant radiologist and radiology registrar. Each case reviewed by both authors and consensus determination of no traumatic abnormality, stable traumatic abnormality or unstable traumatic abnormality noted. CT helical acquisition made from above C1 to below T2. Reconstructions performed by 2 mm contiguous slices in axial, coronal and sagittal planes. Six different CT scanners from three manufacturers of 16, 64 and 128 slice were used. MRI performed with sagittal short T1 inversion recovery, T1 and T2 weighted imaging, axial 3D T2 weighted imaging and gradient recalled echo Siemens Magnetom Symphony 1.5T.</p> <p>Time between measurement of index test and reference standard: time between CT and MRI unclear</p>								
Outcome	<p>Any cervical spinal cord injury (stable and unstable)</p> <p>Unstable injuries only also reported but not extracted as would require MRI to be used as reference standard, as results not given for CT in terms of classifying into stable/unstable injuries based on CT. Unstable injuries defined by Denis 3 column definition as well as any cases requiring urgent surgery (within 5 days of injury) or urgent immobilisation (e.g. halo-traction ring). Other specific unstable injuries also included: flexion teardrop fracture, bilateral locked facets, hangman's fracture, Jefferson fracture and Type 2 dens fracture.</p>								
2x2 table	<p>Any cervical spinal cord injury – CT as index test</p> <table border="1" data-bbox="533 1197 2022 1284"> <tr> <td data-bbox="533 1197 779 1284"></td> <td data-bbox="779 1197 1070 1284">Reference standard +</td> <td data-bbox="1070 1197 1373 1284">Reference standard –</td> <td data-bbox="1373 1197 1619 1284">Total</td> <td data-bbox="1619 1197 2022 1284">Note false positives were not possible using CT + MRI as a</td> </tr> </table>					Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a
	Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a					

Reference	Friesen 2014 ¹⁸					
	Index test +	115	NA	115	reference standard meaning specificity could not be calculated.	
	Index test -	24	67	91		
	Total	139	67	206		
	Any cervical spinal cord injury – MRI as index test					
		Reference standard +	Reference standard -	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.	
	Index test +	98	NA	98		
	Index test -	41	67	108		
	Total	139	67	206		
	Statistical measures	<p>Any cervical spinal cord injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 83.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Any cervical spinal cord injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 71.0</p>				

Reference	Friesen 2014¹⁸
	Specificity: NA PPV: NA NPV: NA
Source of funding	Not reported
Limitations	Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and mean time interval between index test and reference standard unclear – applies to both index tests Indirectness: none – considered to represent head injury population as >75% said to have had brain CT at same time
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Gale 2005¹⁹
Study type	Retrospective
Study methodology	Data source: retrospective review of patients evaluated by Trauma Service Activation at Hospital of Pennsylvania Recruitment: retrospective inclusion of those matching inclusion criteria from single hospital between December 2002 and July 2003
Number of patients	n = 400

Reference	Gale 2005¹⁹
	(n=848 with blunt trauma, of which n=716 had a CT of the cervical spine and n=640 had both CT and plain radiography/X-ray of cervical spine; population was further reduced to n=400 having plain radiography/X-ray and supplemental CT)
Patient characteristics	<p><u>Note: characteristics below given for whole group only (n=1151) and not those analysed (n=400)</u></p> <p>Age, mean (SD): 44.00 (22.08) years</p> <p>Gender (male to female ratio): 64.0% males</p> <p>Ethnicity: not reported</p> <p>Head injury: 84.4% of n=848 blunt trauma patients (excluding those with penetrating injuries) had head CT</p> <p>Mechanism of injury:</p> <ul style="list-style-type: none">• Motor vehicle collision, 42.3%• Fall, 30.5%• Assault, 11.9%• Pedestrian vs. auto, 6.6%• Other, 8.6% <p>GCS score, mean (SD): not reported</p>

Reference	<p>Gale 2005¹⁹</p> <p>Injury Severity Score, mean (SD): 9.37 (10.06)</p> <p>Setting: secondary care – those arriving in hospital with blunt trauma</p> <p>Country: USA</p> <p>Inclusion criteria: blunt trauma patients evaluated by Trauma Service activation between December 2002 and July 2003 – those relevant to review also had X-ray and CT of cervical spine that were complete.</p> <p>Exclusion criteria: penetrating injuries</p> <p>People with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – all underwent head CT so considered a direct population
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p><u>Reference standard</u></p> <p>CT of cervical spine – gold standard for fractures</p>

Reference	Gale 2005¹⁹																			
	<p>Intranet-based electronic medical records reviewed to ascertain which radiographic studies were obtained during their trauma evaluation. Reports of all studies were reviewed and anatomic adequacy of each and its results were recorded in a spreadsheet. Plain cervical spine radiography considered anatomically inadequate if evaluating radiologist dictation included any of the following: study limited to level <T1, cervicothoracic junction not visualised or specific statement of limited or inadequate study because of non-visualisation of the entire cervical spine. Cervical spine CT defined as supplemental if it was performed to attain anatomic completion to T1. Not supplemental if obtained to observe a specific finding or a suspicious region on plain radiography.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and reference standard</p>																			
Outcome	<p>Cervical spine fracture</p> <p>Plain cervical spine radiography considered positive if a specific feature identified or an area on plain films was interpreted as suspicious and warranting further imaging. Negative if no fracture identified and no further imaging recommended. CT considered positive only if a specific fracture was identified.</p>																			
2x2 table	<p>Cervical spine fracture – X-ray as index test</p> <table border="1" data-bbox="539 863 1610 1187"> <thead> <tr> <th data-bbox="539 863 779 954"></th> <th data-bbox="779 863 1072 954">Reference standard +</th> <th data-bbox="1072 863 1373 954">Reference standard –</th> <th data-bbox="1373 863 1610 954">Total</th> </tr> </thead> <tbody> <tr> <td data-bbox="539 954 779 1013">Index test +</td> <td data-bbox="779 954 1072 1013">6</td> <td data-bbox="1072 954 1373 1013">3</td> <td data-bbox="1373 954 1610 1013">9</td> </tr> <tr> <td data-bbox="539 1013 779 1072">Index test –</td> <td data-bbox="779 1013 1072 1072">13</td> <td data-bbox="1072 1013 1373 1072">378</td> <td data-bbox="1373 1013 1610 1072">391</td> </tr> <tr> <td data-bbox="539 1072 779 1187">Total</td> <td data-bbox="779 1072 1072 1187">19</td> <td data-bbox="1072 1072 1373 1187">381</td> <td data-bbox="1373 1072 1610 1187">400</td> </tr> </tbody> </table>					Reference standard +	Reference standard –	Total	Index test +	6	3	9	Index test –	13	378	391	Total	19	381	400
	Reference standard +	Reference standard –	Total																	
Index test +	6	3	9																	
Index test –	13	378	391																	
Total	19	381	400																	
Statistical measures	<p>Cervical spine fracture – X-ray as index test: reported in paper</p> <p>Sensitivity: 31.6%</p>																			

Reference	Gale 2005¹⁹
	Specificity: 99.2% PPV: 66.7% NPV: 96.7%
Source of funding	Not reported
Limitations	Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test and unclear time interval between index test Indirectness: serious – outcome limited to fractures rather than any cervical spine injury
Comments	None

Reference	Gharekhanloo 2021²⁰
Study type	Prospective
Study methodology	Data source: prospective study of trauma patients at an emergency department. Recruitment: not reported.
Number of patients	n = 220 (n=210 had normal CT scans, n=10 had cervical spine injury on CT scans).
Patient characteristics	Age, mean (SD): 38.25 (5.13) years (35% between 26 and 35 years) Gender (male to female ratio): 157/63

Reference	Gharekhanloo 2021 ²⁰
	<p data-bbox="546 284 835 317">Ethnicity: not reported</p> <p data-bbox="546 400 1753 434">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head.</p> <p data-bbox="546 517 1473 550">Mechanism of injury: car accidents (64%) and falls from height (17.7%).</p> <p data-bbox="546 633 1229 667">GCS score at initial trauma, mean (SD): not reported</p> <p data-bbox="546 750 965 783">Injury Severity Score, median: 5</p> <p data-bbox="546 866 1133 900">Setting: Emergency department of a Hospital</p> <p data-bbox="546 983 719 1016">Country: Iran</p> <p data-bbox="546 1099 1469 1133">Inclusion criteria: low-risk status based on international NEXUS criteria.</p> <p data-bbox="546 1216 1039 1249">Exclusion criteria: penetrating trauma.</p>

Reference	Gharekhanloo 2021²⁰
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>Plain radiography</p> <p><u>Reference standard</u></p> <p><u>Cervical CT scan</u></p> <p>Plain radiographs were obtained in anteroposterior, lateral and odontoid views. Cervical CT was performed using a 16-slice multidetector CT scanner in a supine position. Images started with lateral scout images from the foramen magnum to the junction of the C7-T1 vertebral Junction. The standard scan protocols included the voltage of 130kV, collimation of 1mm, pitch of 0.66, and tube current-time product of 200mAs. Coronal and sagittal reformation images were reconstructed using 1.5-mm intervals from an axial source on a standard workstation.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and reference standard.</p>
Outcome	<p>Cervical spine injury was defined as subluxation/dislocation or acute fracture or both.</p> <p>Interpretation of plain radiographs and cervical CT images performed by 2 experienced, board-certified radiologists who were blinded to the results. A clinically significant injury was determined based on the neurosurgical recommendation of one or more interventions, operation and rigid cervical collar or halo application.</p>
2x2 table	Cervical spine injury – Plain radiography

Reference	Gharekhanloo 2021 ²⁰				
		Reference standard +	Reference standard -	Total	
	Index test +	4	6	10	
	Index test -	6	204	210	
	Total	10	210	220	
Statistical measures	<p>Cervical spine injury</p> <p>Sensitivity: 40%</p> <p>Specificity: 100%</p> <p>PPV: 60%</p> <p>NPV: infinity</p>				
Source of funding	None				
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear time interval between index test and reference standard.</p> <p>Indirectness: unclear if head injury patients.</p>				
Comments	Only 10 patients had cervical spine injury on the reference standard.				

Reference	Goodnight 2008²¹
Study type	Retrospective
Study methodology	Data source: retrospective review of trauma registry (general database of all trauma admission) of a single American College of Surgeons verified Level 1 trauma centre Recruitment: retrospective chart review from a single trauma centre of admissions between 2003 and 2004
Number of patients	n = 379 (n=1809 with trauma had CT of cervical spine, with n=379 subsequently included as they also had flexion-extension radiography performed once fracture had been ruled out on CT)
Patient characteristics	Age, mean (SD): 39 (19) years Gender (male to female ratio): 63% males Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: 53.0% motor vehicle crash GCS score at initial trauma, mean (SD): not reported Injury Severity Score, median: 5

Reference	Goodnight 2008²¹
	<p>Setting: secondary care – trauma centre database review</p> <p>Country: USA</p> <p>Inclusion criteria: blunt mechanism of injury; and received both CT of cervical spine and follow-up flexion/extension radiographs for continued cervical spine pain</p> <p>Exclusion criteria: neurologic deficits consistent with cervical cord injury; obtunded patients; penetrating mechanism of injury; and age <18 years</p> <p>Adults with blunt trauma and suspected cervical spine injury – continued cervical spine pain specifically</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>Flexion-extension X-ray of cervical spine</p> <p>Helical CT of cervical spine</p> <p><u>Reference standard</u></p> <p>All available evidence, including MRI in some patients. Unclear follow-up for those that did not have MRI.</p>

Reference	Goodnight 2008²¹			
	<p>For CT, helical CT technique used with 1.5 mm collimation helical scanning at pitch of 1.5 from T1 to occiput performed in two acquisitions. Axial images reconstructed with bone algorithm at 1.5 mm intervals with sagittal and coronal reconstructions. MRI considered gold standard for ligamentous injuries. Obtained as confirmatory study in each patient with negative CT and positive flexion/extension radiograph. Radiologists routinely assessed CT scans for ligamentous injury.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and reference standard, unclear follow-up for those that did not have MRI.</p>			
Outcome	<p>Ligamentous injury of the cervical spine</p> <p>Suspicion of ligamentous injury on CT based on interpretation of board-certified radiologists. Findings raising suspicion included paravertebral soft tissue swelling, widening or subluxation of facet joints, focal kyphosis with splaying of spinolaminar distances and abnormal widening of articulations at cranio-cervical junction. Report data obtained from radiology department database. CT findings classified into negative of cervical spine injury, suspicious for ligamentous injury and technically inadequate based on original reports.</p>			
2x2 table	Ligamentous cervical spine injury – Flexion-extension X-ray as index test			
		Reference standard +	Reference standard –	Total
	Index test +	6	10	16
	Index test –	0	363	363
	Total	6	373	379
	Ligamentous cervical spine injury – Helical CT as index test			

Reference	Goodnight 2008 ²¹				
		Reference standard +	Reference standard -	Total	
	Index test +	6	13	19	
	Index test -	0	360	360	
	Total	6	373	379	
Statistical measures	<p>Ligamentous cervical spine injury – Flexion-extension X-ray as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 97.3%</p> <p>PPV: 37.5%</p> <p>NPV: 100.0%</p> <p>Ligamentous cervical spine injury – Helical CT as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 96.5%</p> <p>PPV: 31.6%</p> <p>NPV: 100.0%</p>				
Source of funding	Not reported				

Reference	Goodnight 2008²¹
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard was interpreted without knowledge of index test, unclear time interval between index test and reference standard and likely that reference standard components different between patients – applies to both index tests</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, population where those with confirmed fractures were excluded meaning may differ from population presenting without any prior imaging, outcome limited to ligamentous injuries and unclear if reference standard included a 2 week follow-up period</p>
Comments	Population had already been ruled out for cervical fracture so may represent different population to those initially presenting with no imaging.

Reference	Griffen 2003²²
Study type	Retrospective
Study methodology	<p>Data source: TRACS database from single level 1 trauma centre</p> <p>Recruitment: retrospective review of database from single level 1 trauma centre between November 2000 and October 2001</p>
Number of patients	n = 1199(n=3018 blunt trauma patients with risk of cervical spine injury identified, with n=1199 subsequently included as they had both plain radiography/X-ray and CT of cervical spine)
Patient characteristics	<p>Average age: 39.4 years</p> <p>Gender (male to female ratio): 65.0% males</p>

Reference	Griffen 2003 ²²
	<p data-bbox="546 229 835 261">Ethnicity: not reported</p> <p data-bbox="546 347 1747 379">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="546 466 983 497">Mechanism of injury: not reported</p> <p data-bbox="546 584 860 616">Average GCS score: 13</p> <p data-bbox="546 702 994 734">Average Injury Severity Score: 8.4</p> <p data-bbox="546 820 1323 852">Setting: secondary care – review of trauma centre database</p> <p data-bbox="546 938 730 970">Country: USA</p> <p data-bbox="546 1056 1991 1114">Inclusion criteria: adults with blunt trauma between November 200 and October 2001; and having X-ray and CT of cervical spine</p> <p data-bbox="546 1200 1644 1232">Exclusion criteria: inadequate radiographs or a recommendation for cervical CT scan</p>

Reference	Griffen 2003²²
	Adults with blunt trauma and suspected cervical spine injury
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p> <p>Unclear, possibly all imaging/follow-up</p> <p>Institutional protocol included initial physical exam of cervical spine. Those with reliable examinations and no neck pain or tenderness were clinically cleared by physical exam alone. Stabilisation collars removed and no further evaluation of cervical spine performed. Patients with neck tenderness, neurologic deficits, altered mental status or distracting pain from other injuries all underwent standard three-view cervical spine radiography and cervical spine CT scan. If these indicate negative results, cervical collar left in place until a reliable physical examination can be performed. Patients returning to clinic with continued cervical tenderness have flexion-extension radiographs to rule out ligamentous injuries. Those with persisting tenderness and negative radiography/CT including flexion-extension views after 1 month and those that develop any neurologic deficit referred to spine service for final clearance.</p> <p>Time between measurement of index test and reference standard: unclear duration between index tests and other imaging/final diagnosis being confirmed</p>
Outcome	Cervical spine injury – poorly defined
2x2 table	Cervical spine injury – X-ray as index test

Reference	Griffen 2003 ²²				
		Reference standard +	Reference standard -	Total	Limited reporting of raw data means only sensitivity can be calculated.
	Index test +	75	NR	NR	
	Index test -	41	NR	NR	
	Total	116	1083	1199	
	Cervical spine injury – CT as index test				
		Reference standard +	Reference standard -	Total	Limited reporting of raw data means only sensitivity can be calculated.
	Index test +	116	NR	NR	
	Index test -	0	NR	NR	
	Total	116	1083	1199	
	Statistical measures	Cervical spine injury – X-ray as index test: calculated using excel sheet Sensitivity: 65.0% Specificity: NR			

Reference	Griffen 2003²²
	<p>PPV: NR</p> <p>NPV: NR</p> <p>Cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 100.0%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if index test and reference standard interpreted without knowledge of the other, unclear time interval between index test and reference standard and likely that reference standard components differed between patients – applies to both index tests</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard included a 2 week follow-up period</p>
Comments	None

Reference	Inaba 2016²⁷
Study type	Prospective
Study methodology	Data source: multi-centre prospective observational trial performed at 18 level 1 and 2 trauma centres

Reference	Inaba 2016²⁷
	Recruitment: multi-centre across 18 level 1 and 2 trauma centres in North America through Western Trauma Association Multi-institutional Trials group
Number of patients	n = 10,276 (n=10,765 patients matched entry criteria, with n=489 subsequently excluded due to previous spinal surgery, outside hospital transfer or both; leaving n=10,276 analysed in the study)
Patient characteristics	<p>Age, mean (range): 48.1 (18.0-110.0) years</p> <p>Gender (male to female ratio): 66.7% males</p> <p>Ethnicity: not reported</p> <p>Head injury: 3.6% said to be unevaluable due to a traumatic brain injury (TBI) – unclear if/proportion of others that were evaluable and had suspected or confirmed head injury</p> <p>Mechanism of injury:</p> <ul style="list-style-type: none"> • Motor vehicle collision, 30.0% • Ground level fall, 20.9% • Fall from height, 11.9% • Other, 10.2% • Automobile vs. pedestrian, 9.0% • Assault, 7.0%

Reference	Inaba 2016 ²⁷
	<ul style="list-style-type: none">• Motorcycle collision, 6.9%• Bicycle vs. automobile, 3.8% <p>GCS score at admission, median (IQR): 15 (14-15)</p> <p>Injury Severity Score, median (IQR): 9 (4-16)</p> <p>Neurological examination:</p> <ul style="list-style-type: none">• Unevaluable, 45.3%<ul style="list-style-type: none">○ TBI, 3.6%○ Distracting injury, 4.3%○ Intoxicated/intubated, 11.4%○ Combination, 26.0%• Evaluable, 54.7%<ul style="list-style-type: none">○ No deficit, 49.0%○ Motor deficit, 2.4%○ Sensory deficit, 1.8%○ Motor/sensory deficit, 1.5%• Type of imaging:<ul style="list-style-type: none">○ CT, 100.0%○ MRI, 9.2%○ Plain X-ray, 1.4%○ Flexion-extension X-ray, 0.4% <p>Hospital length of stay, median (IQR): 2 (1-6) days</p>

Reference	Inaba 2016²⁷
	<p>ICU length of stay, median (IQR): 0 (0-1.4) days</p> <p>Setting: secondary care – multiple trauma centres</p> <p>Country: USA</p> <p>Inclusion criteria: blunt trauma; ≥18 years; and failing NEXUS 2 low risk criteria</p> <p>Exclusion criteria: transferred from an outside facility; had a history of spinal instrumentation; did not undergo diagnostic imaging with CT Scan of their C-spine; and cervical spine imaging from outside hospitals</p> <p>Adults with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT scan of cervical spine</p> <p><u>Reference standard</u></p> <p>Final diagnosis at discharge, including results of all imaging and operative findings.</p>

Reference	Inaba 2016²⁷				
	<p>Any additional imaging including use of MRI was at discretion of treating clinician. History and physical exam (NEXUS criteria, presence or absence of midline C-spine tenderness and results of neurological examination) performed by senior resident or faculty member using structured form. All imaging interpreted by attending radiologist blinded to study case report form contents and final attending radiologist read was used in analysis.</p> <p>Time between measurement of index test and reference standard: median length of stay was 2 (IQR 1-6) days – shorter follow-up period than 2 weeks as in protocol (indirectness).</p>				
Outcome	Clinically significant cervical spine fracture – an abnormal or equivocal finding observed on either CT or MRI consistent with acute traumatic injury was necessary, along with one of three active interventions: surgical stabilization, Halo Orthotic placement or use of a Cervical-Thoracic Orthotic.				
2x2 table	CT scan of cervical spine as index test – clinically significant cervical spine fracture				
		Reference standard +	Reference standard –	Total	Raw data incompletely reported but calculated from sensitivity/specificity etc. reported in the paper
	Index test +	195	907	1102	
	Index test –	3	9171	9174	
	Total	198	10,078	10,276	
Statistical measures	<p>CT scan of cervical spine as index test – clinically significant cervical spine fracture: reported in the paper</p> <p>Sensitivity: 98.5%</p> <p>Specificity: 91.0%</p> <p>PPV: 17.8%</p> <p>NPV: 99.97%</p>				

Reference	Inaba 2016²⁷
Source of funding	Reported that there were no funding disclosures
Limitations	<p>Risk of bias: very serious – convenience sampling rather than consecutive patients enrolled, reference standard of final diagnosis at discharge does not involve a period of at least 2 weeks since admission, unclear if reference standard was interpreted without knowledge of index test and likely that reference standard different slightly between patients (e.g. any further tests performed)</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and reference standard indirectness as outcome only includes fractures and does not involve a period of 2 weeks follow-up as specified in the protocol</p>
Comments	None

Reference	Lau 2018²⁸
Study type	Retrospective
Study methodology	<p>Data source: retrospective review of data from level 1 trauma centre</p> <p>Recruitment: retrospective review of level 1 trauma centre data between 1st January 2008 and 31st December 2012</p>
Number of patients	<p>n = 63</p> <p>(n=66 met inclusion criteria, with n=3 of these excluded based on exclusion criteria; leaving n=63 included in the analysis)</p>
Patient characteristics	<p>Age, mean (SD): 42.3 (18.2) years</p> <p>Gender (male to female ratio): 90.5% males</p>

Reference	Lau 2018 ²⁸
	<p data-bbox="546 288 667 316">Ethnicity:</p> <ul data-bbox="595 349 875 485" style="list-style-type: none">• Chinese, 63.5%• Malaysian, 11.1%• Indian, 19.0%• Other, 6.4% <p data-bbox="546 571 1957 635">Head injury: unclear if all or most had head injury but suggests all may have undergone assessment for brain injuries (limited information)</p> <p data-bbox="546 721 819 748">Mechanism of injury:</p> <ul data-bbox="595 782 1066 1086" style="list-style-type: none">• Fall from height, 17.5%• Fall from standing height, 19.0%• Road traffic accident:<ul data-bbox="689 890 1055 1018" style="list-style-type: none">○ Motorcyclist, 31.7%○ Car, 15.9%○ Lorry/van, 7.9%○ Cyclist/pedestrian, 3.2%• Direct blunt force, 4.8% <p data-bbox="546 1173 1229 1200">GCS score at initial trauma, mean (SD): not reported</p> <p data-bbox="546 1289 1184 1316">Injury Severity Score, mean (range): not reported</p>

Reference	Lau 2018 ²⁸
	<p data-bbox="546 288 842 316">Suspected injury level:</p> <ul data-bbox="595 349 936 448" style="list-style-type: none"><li data-bbox="595 349 936 376">• Cervical spine, 81.0%<li data-bbox="595 381 936 408">• Thoracic spine, 22.2%<li data-bbox="595 413 936 440">• Lumbar spine, 4.8% <p data-bbox="546 536 689 563">Neurology:</p> <ul data-bbox="595 596 1003 767" style="list-style-type: none"><li data-bbox="595 596 927 624">• Normoreflexia, 36.4%<li data-bbox="595 628 1003 655">• Upper limb areflexia, 50.9%<li data-bbox="595 660 1003 687">• Lower limb areflexia, 61.8%<li data-bbox="595 692 920 719">• Lax anal tone, 41.8%<li data-bbox="595 724 965 751">• Unable to assess, 12.7% <p data-bbox="546 855 1070 882">Setting: secondary care – trauma centre</p> <p data-bbox="546 970 801 997">Country: Singapore</p> <p data-bbox="546 1086 1626 1114">Inclusion criteria: blunt trauma; obtunded (GCS score ≤ 8); and admitted to ICU unit.</p> <p data-bbox="546 1203 1980 1300">Exclusion criteria: incomplete data due to electronic downtime during admission; transferred from another hospital with CT or MRI scans already performed; requiring emergency surgery following CT scan as a form of resuscitation; and would not be able to perform an MRI scan due to medical reasons</p>

Reference	Lau 2018²⁸
	Obtunded people with blunt trauma and suspected cervical spine injury
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury but suggests all may have undergone assessment for brain injuries (limited information)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p> <p>MRI reported in paper to be reference standard, but not in line with this review protocol. Therefore, data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>Based on clinical workflow at the institution, all suffering blunt injuries and that are obtunded are evaluated with CT on emergency basis once initial resuscitation performed. CT performed as non-contrast study for head, cervical spine, thorax, abdomen and pelvis with 10 mm axial cuts. Purpose is to assess for cervical spine injuries at the same time as brain and visceral injuries. All apart for those requiring emergency surgery will be scheduled for interval MRI scan of cervical spine for clearance of injuries as part of standard clinical workflow. MRI performed without contrast within 48 h of admission after patient condition has stabilised. Cervical immobilisation only removed after CT and MRI image reviewed by attending spine or trauma consultant and following confirmation of the final report issued by senior radiologist.</p>

Reference	Lau 2018²⁸
	Time between measurement of index test and reference standard: CT performed when initial resuscitation performed and MRI performed within 48 h of admission after condition has stabilised.
Outcome	Cervical spine injuries – poorly defined but appears to include bony and soft tissue injuries
2x2 table	Data insufficiently reported to complete 2x2 tables. 7 patients reported to have findings on MRI with no positive findings on CT. Reported that no patients within findings on CT were negative on MRI.
Statistical measures	<p>Cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 87.2%</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Any cervical spinal cord injury – MRI as index test: calculated using statement that none that were positive on CT were negative on MRI</p> <p>Sensitivity: 100%</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>
Source of funding	Not reported

Reference	Lau 2018²⁸
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and mean time interval between index test and reference standard possibly at least 48 h – applies to both index tests</p> <p>Indirectness: serious – all included were at obtunded and admitted to ICU representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p>
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Lee 2001²⁹
Study type	Retrospective
Study methodology	<p>Data source: retrospective review of patients from single level 1 trauma centre emergency room</p> <p>Recruitment: retrospective review of single level 1 trauma centre data between January 1999 and June 2000</p>
Number of patients	n = 604(n=3684 adult trauma patients underwent screening of cervical spine, with n=604 included in the analysis as they had both conventional radiography and helical CT)
Patient characteristics	<p>Age, mean (SD): not reported</p> <p>Gender (male to female ratio): 50.7% males</p> <p>Ethnicity: not reported</p>

Reference	Lee 2001 ²⁹
	<p>Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p>Mechanism of injury: not reported</p> <p>GCS score at initial trauma, mean (SD): not reported</p> <p>Injury Severity Score, mean (SD): not reported</p> <p>Setting: secondary care – data from a trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: adults suffering trauma presenting to ED; and underwent cervical spine imaging with both plain radiography and helical CT</p> <p>Exclusion criteria: those who only had plain radiography or only had helical CT of cervical spine, or where imaging were not available for comparison</p> <p>Adults with trauma and suspected cervical spine injury</p>

Reference	Lee 2001²⁹				
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided				
Index test(s) and reference standard	<p><u>Index test</u> X-ray of cervical spine</p> <p><u>Reference standard</u> Helical CT scan</p> <p>Plain radiographs included standard four views (antero-posterior, lateral, and swimmers and open-mouthed odontoid views). Helical CT involved 1 mm collimation helical scanning from foramen magnum level to C3 vertebral body and 3 mm collimation from C3 to T1. Contiguous axial images obtained with bone and soft tissue algorithms. Sagittal and coronal reconstructions also obtained. All studies reviewed by radiology resident and neuroradiologist.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index test and reference standard</p>				
Outcome	Cervical spine fracture				
2x2 table	Cervical spine fracture – X-ray as index test				
		Reference standard +	Reference standard -	Total	Raw data given only for individual fractures (with each patient possibly having more than one fractures – 36)
	Index test +	12	NR	NR	
	Index test -	24	NR	NR	

Reference	Lee 2001 ²⁹				
	Total	36	NR	604 patients (raw data given for fractures – some patients had more than one fracture)	fractures on CT in 30 patients) Incompletely reported meaning specificity not reported and calculation not possible.
Statistical measures	<p>Cervical spine fracture – X-ray as index test (individual fractures identified not patients with fractures): reported in paper</p> <p>Sensitivity: 33.3%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p>				
Source of funding	Not reported				
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test and unclear time interval between index test and reference standard</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, outcome limited to fractures rather than any cervical spine injury, and results interpreted at fracture level not patient level (patients could have more than one fracture and these included individually in analysis)</p>				

Reference	Lee 2001²⁹
Comments	Analyses sensitivity at fracture level and not patient level (each patient could have more than one fracture and these were included separately in calculation of sensitivity)

Reference	Malhotra 2018³⁰
Study type	Retrospective
Study methodology	Data source: radiology database of single tertiary health system and level 1 trauma centre Recruitment: retrospective review of database of single tertiary health system and level 1 trauma centre between February 2013 and November 2015
Number of patients	n = 1080 (n=1271 with blunt cervical spine trauma underwent both a CT and MRI of cervical spine, with n=191 subsequently excluded based on incomplete medical record information, limited CT studies or absent CT reports usually from transferred patients; leaving n=1080 included in the analysis)
Patient characteristics	Age, mean (range): 57 (18-93) years Gender (male to female ratio): 55.0% males Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head

Reference	Malhotra 2018 ³⁰
	<p data-bbox="546 288 819 320">Mechanism of injury:</p> <ul data-bbox="595 347 1167 632" style="list-style-type: none"><li data-bbox="595 347 976 379">• Fall from standing, 43.6%<li data-bbox="595 384 1099 416">• Motor vehicle collision-auto, 20.8%<li data-bbox="595 421 949 453">• Fall from height, 19.5%<li data-bbox="595 458 1160 489">• Motor vehicle collision-pedestrian, 6.7%<li data-bbox="595 494 824 526">• Assault, 4.7%<li data-bbox="595 531 1167 563">• Motor vehicle collision-motorcycle, 1.3%<li data-bbox="595 568 875 600">• Sport injury, 2.6%<li data-bbox="595 604 902 636">• Falling object, 0.7% <p data-bbox="546 715 1232 746">GCS score at initial trauma, mean (SD): not reported</p> <p data-bbox="546 831 1187 863">Injury Severity Score, mean (range): not reported</p> <p data-bbox="546 948 1200 979">Setting: secondary care – trauma centre database</p> <p data-bbox="546 1064 730 1096">Country: USA</p> <p data-bbox="546 1181 1955 1244">Inclusion criteria: adults with suspected blunt trauma to cervical spine; and underwent CT followed by MRI of cervical spine within 48 h</p>

Reference	Malhotra 2018³⁰
	<p>Exclusion criteria: CT study was non-diagnostic due to patient motion or their medical record was incomplete</p> <p>Adults with suspected blunt trauma to cervical spine</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p> <p>MRI reported in paper to be reference standard, but not in line with this review protocol. Therefore, data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>CT cervical spine images acquired on 64-detector scanners with 1.25 mm slice helical acquisition without intravenous contrast and reformatted in coronal and sagittal planes. Siemens 1.5T and 3T magnets used for MRI scanning, without intravenous contrast using trauma protocol sequences including sagittal T1 FSE, axial and sagittal T2 FSE, sagittal STIR and sagittal GRE sequences.</p> <p>CT studies reviewed by neuroradiology fellow to classify into negative or positive for acute traumatic injury based on final report given by ED at time of scan. Studies that were unequivocally negative for injury were classified as negative CT. Studies were positive on CT if impressions included any of the following features: fractures of occipital condyles or C1-C7 vertebral bodies, disc space widening, vertebral subluxation, prevertebral or paravertebral oedema and haematoma, epidural haematoma, cord haematoma or new disc herniation.</p>

Reference	Malhotra 2018³⁰			
	<p>On MRI, studies were positive if contained any of the following features: fractures of occipital condyles or C1-C7 vertebral bodies, osseous oedema or contusion, ligamentous injury or paravertebral muscle strain, spinal cord oedema or haemorrhage, epidural/subdural haematoma, new or acute disc herniation, and prevertebral oedema or haematoma. MRI studies interpreted unequivocally as negative for any of the above findings were classified as negative MRI. MRI findings were confirmed by neuroradiology faculty with 8 years' experience blinded to patient characteristics, outcome, management and report contents other than the impression.</p> <p>Time between measurement of index test and reference standard: CT performed and MRI performed within 48 h.</p>			
Outcome	Any cervical spine injury – including osseous and ligamentous injuries			
2×2 table	Any cervical spine injury – CT as index test			
	Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
Index test +	368	NA	368	
Index test –	149	563	712	
Total	517	563	1080	
	Any cervical spine injury – MRI as index test			
	Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
Index test +	427	NA	427	
Index test –	90	563	653	
Total	517	563	1080	

Reference	Malhotra 2018 ³⁰
Statistical measures	<p>Any cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 71.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Any cervical spine injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 83.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>
Source of funding	Stated that no funding was received
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and mean time interval between index test and reference standard likely at least 48 h – applies to both index tests</p> <p>Indirectness: serious – head injury not mentioned and unclear if all or most had head injury</p>
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Mathen 2007³¹
Study type	Prospective
Study methodology	Data source: performed at single level 1 trauma centre Recruitment: unblinded prospective consecutive series design at a single level 1 trauma centre between October 2004 and February 2005. All presenting to institution prospectively enrolled into study protocol.
Number of patients	n = 667(n=682 matching inclusion criteria, with n=6 dying before cervical spine evaluation and n=9 only having CT rather than both X-ray and CT excluded from the analysis; leaving n=667 included)
Patient characteristics	Average age: 35.4 years Gender (male to female ratio): not reported Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: <ul style="list-style-type: none"> • Motor vehicle collision, 48.7% • Pedestrian hit by auto, 14.4% • Falls, 13.5% Average GCS score score: 13.2

Reference	Mathen 2007³¹
	<p>Injury Severity Score, mean (SD): not reported</p> <p>Setting: secondary care – trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: not meeting NEXUS low-risk criteria; and undergoing multi-slice CT and 3-view plain radiography of cervical spine</p> <p>Exclusion criteria: death before completion of both CT and plain radiography of cervical spine</p> <p>People with trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p>Multi-slice CT of cervical spine</p> <p><u>Reference standard</u></p> <p>Final diagnosis of cervical spine injury based on all prospectively collected clinical data and imaging results, unclear follow-up duration</p>

Reference	Mathen 2007³¹																			
	<p>All CTs (occiput to T1) performed using four-channel CT scanner with collimation of 2 mm. Coronal and sagittal reformation images using 1.5 mm to 2 mm intervals reconstructed from axial source images. Three-view plain radiography (X-ray) included anterior-posterior, lateral and odontoid views. Additional views (swimmers, obliques) performed at discretion of attending radiologist. Final radiographic interpretation of CT and plain films performed by board-certified radiologists.</p> <p>Time between measurement of index test and reference standard: unclear time interval between index tests and subsequent tests/final confirmed diagnosis</p>																			
Outcome	<p>Any acute cervical spine injury – acute fracture or subluxation, or both</p> <p>and</p> <p>Clinically significant cervical spine injury – requiring surgery or long-term stabilisation with a collar or halo</p>																			
2x2 table	<p>Any acute cervical spine injury – X-ray as index test</p> <table border="1" data-bbox="530 957 1612 1283"> <thead> <tr> <th data-bbox="530 957 779 1050"></th> <th data-bbox="779 957 1075 1050">Reference standard +</th> <th data-bbox="1075 957 1375 1050">Reference standard –</th> <th data-bbox="1375 957 1612 1050">Total</th> </tr> </thead> <tbody> <tr> <td data-bbox="530 1050 779 1109">Index test +</td> <td data-bbox="779 1050 1075 1109">27</td> <td data-bbox="1075 1050 1375 1109">16</td> <td data-bbox="1375 1050 1612 1109">43</td> </tr> <tr> <td data-bbox="530 1109 779 1168">Index test –</td> <td data-bbox="779 1109 1075 1168">33</td> <td data-bbox="1075 1109 1375 1168">591</td> <td data-bbox="1375 1109 1612 1168">624</td> </tr> <tr> <td data-bbox="530 1168 779 1283">Total</td> <td data-bbox="779 1168 1075 1283">60</td> <td data-bbox="1075 1168 1375 1283">607</td> <td data-bbox="1375 1168 1612 1283">667</td> </tr> </tbody> </table>					Reference standard +	Reference standard –	Total	Index test +	27	16	43	Index test –	33	591	624	Total	60	607	667
	Reference standard +	Reference standard –	Total																	
Index test +	27	16	43																	
Index test –	33	591	624																	
Total	60	607	667																	

Reference	Mathen 2007 ³¹			
	Any acute cervical spine injury – CT as index test			
		Reference standard +	Reference standard –	Total
	Index test +	60	3	63
	Index test –	0	604	604
	Total	60	607	667
	Clinically significant cervical spine injury – X-ray as index test			
		Reference standard +	Reference standard –	
	Index test +	12	31	43
	Index test –	15	609	624
	Total	27	640	667
	Clinically significant cervical spine injury – CT as index test			
		Reference standard +	Reference standard –	
	Index test +	27	36	63
Index test –	0	604	604	
Total	27	640	667	

Reference	Mathen 2007 ³¹
Statistical measures	<p>Any acute cervical spine injury – X-ray as index test: reported in paper</p> <p>Sensitivity: 45.0%</p> <p>Specificity: 97.4%</p> <p>PPV: 62.8%</p> <p>NPV: 94.7%</p> <p>Any acute cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 99.5%</p> <p>PPV: 95.2%</p> <p>NPV: 100.0%</p> <p>Clinically significant cervical spine injury – X-ray as index test: calculated using excel sheet</p> <p>Sensitivity: 44.0%</p> <p>Specificity: 95.0%</p> <p>PPV: 28.0%</p> <p>NPV: 98.0%</p>

Reference	Mathen 2007³¹
	<p>Clinically significant cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 94.0%</p> <p>PPV: 43.0%</p> <p>NPV: 100.0%</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if reference standard interpreted without knowledge of index test, unclear interval between index test and reference standard and unclear if reference standard contained the same components for all patients – applies to both index tests</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard included a 2 week follow-up period</p>
Comments	None

Reference	Nguyen 2005³³
Study type	Prospective
Study methodology	<p>Data source: observational study at level 1 trauma centre hospital with data recorded prospectively</p> <p>Recruitment: prospective of all patients with trauma and undergoing imaging across a 70-day period</p>
Number of patients	n = 112 (n=78 in low risk group and n=34 in high risk group)

Reference	Nguyen 2005³³
	(n=219 patients meeting inclusion criteria for the paper, with n=112 analysed as they had both plain radiography and CT of the cervical spine)
Patient characteristics	<p>Age, range: 2-89 years for low risk group and 11-88 years for high risk group</p> <p>Gender (male to female ratio): 47.4% males in low risk group and 64.7% males in high risk group</p> <p>Ethnicity: not reported</p> <p>Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p>Mechanism of injury: not reported</p> <p>GCS score at initial trauma, mean (SD): not reported</p> <p>Injury Severity Score, mean (SD): not reported</p> <p>Setting: secondary care – trauma centre hospital</p> <p>Country: USA</p>

Reference	Nguyen 2005³³
	<p>Inclusion criteria: patients with blunt trauma; and underwent imaging of cervical spine</p> <p>Exclusion criteria: not reported</p> <p>Patients with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p> <p>Diagnosis based on final reports including all imaging, unclear duration of follow-up</p> <p>Treating physicians ordered films at their discretion. All major trauma patients screened with standard 3-view cervical spine radiography (cross-table lateral, antero-posterior and odontoid views) and CT. Cervical spine CT performed using Siemens Somatom CT scanner (3 mm slices, four detector rows) with soft tissue window and bone window with sagittal and coronal reconstructions. Injury status determined based on all radiographic studies reviewed and final report.</p> <p>Time between measurement of index test and reference standard: unclear duration between index tests and other imaging/final diagnosis being confirmed</p>

Reference	Nguyen 2005³³				
Outcome	Cervical spine fractures – provides results separately for risk which are extracted separately as strata based on risk in review protocol				
2x2 table	Cervical spine fracture – X-ray as index test (low-risk group)				
		Reference standard +	Reference standard –	Total	Sensitivity not applicable as none in this group had fracture.
	Index test +	0	0	0	
	Index test –	0	78	78	
	Total	0	78	78	
	Cervical spine fracture – CT as index test (low-risk group)				
		Reference standard +	Reference standard –	Total	Sensitivity not applicable as none in this group had fracture.
	Index test +	0	0	0	
	Index test –	0	78	78	
	Total	0	78	78	
	Cervical spine fracture – X-ray as index test (high risk group)				
		Reference standard +	Reference standard –	Total	Raw data incompletely reported but missing values calculated using excel sheet
	Index test +	14	1	15	

Reference	Nguyen 2005 ³³				
	Index test –	1	18	19	and reported sensitivity/specificity in paper
	Total	15	19	34	
	Missed injury was non-displaced fracture through C7 left facet. No soft tissue abnormality associated with it and no misalignment.				
	Cervical spine fracture – CT as index test (high risk group)				
		Reference standard +	Reference standard –	Total	Raw data incompletely reported but missing values calculated using excel sheet and reported sensitivity/specificity in paper
	Index test +	15	0	15	
Index test –	0	19	19		
Total	15	19	34		
Statistical measures	<p>Cervical spine fracture – X-ray as index test (low risk group): reported in paper (apart from NPV which was calculated using excel sheet)</p> <p>Sensitivity: NA</p> <p>Specificity: 100.0%</p> <p>PPV: NA</p> <p>NPV: 100.0%</p>				

Reference	Nguyen 2005 ³³
	<p>Cervical spine fracture – CT as index test (low risk group): reported in paper (apart from NPV which was calculated using excel sheet)</p> <p>Sensitivity: NA</p> <p>Specificity: 100.0%</p> <p>PPV: NA</p> <p>NPV: 100.0%</p> <p>Cervical spine fracture – X-ray as index test (high risk group): reported in paper (apart from NPV and PPV which were was calculated using excel sheet)</p> <p>Sensitivity: 93.3%</p> <p>Specificity: 95.0%</p> <p>PPV: 94.0%</p> <p>NPV: 95.0%</p> <p>Cervical spine fracture – CT as index test (high risk group): reported in paper (apart from NPV and PPV which were was calculated using excel sheet)</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 100.0%</p>

Reference	Nguyen 2005³³
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if index test and reference standard interpreted without knowledge of the other, unclear time interval between index test and reference standard and likely that reference standard components differed between patients – applies to both index tests</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, outcome focuses only on fractures and unclear if reference standard included a 2 week follow-up period</p>
Comments	None

Reference	Novick 2018³⁵
Study type	Retrospective
Study methodology	<p>Data source: retrospective review of data from single level 1 trauma centre serving population of 1.4 million. Trauma registry queried for data and cross-referenced with radiology record system and main hospital medical record system.</p> <p>Recruitment: retrospective review of those matching inclusion criteria from single level 1 trauma centre between 1st January 2008 and 31st December 2015.</p>
Number of patients	<p>n = 241</p> <p>(included n=241 that had both CT and MRI of cervical spine – flow of patients and those excluded unclear)</p>
Patient characteristics	Age, mean (range): 43.9 (5-93) years

Reference	Novick 2018 ³⁵
	<p data-bbox="546 229 1120 260">Gender (male to female ratio): 60.2% males</p> <p data-bbox="546 347 835 378">Ethnicity: not reported</p> <p data-bbox="546 466 1944 528">Head injury: unclear if all or most had head injury – 17% reported to have closed head injury, but unclear for others if head injury was part of the injury mechanism</p> <p data-bbox="546 616 819 646">Mechanism of injury:</p> <ul data-bbox="595 675 1037 1098" style="list-style-type: none">• Assault, 3.3%• Cyclist, 2.1%• Fall from standing, 20.3%• Fall >1 m, 6.2%• Fall stairs, 6.6%• Hanging, 1.2%• Motorcycle crash, 2.1%• Motor vehicle crash, 45.6%• Sports-related, 3.3%• Struck in head, 0.8%• Pedestrian struck, 7.9%• Gunshot wound to neck, 0.4% <p data-bbox="546 1185 1232 1216">GCS score at initial trauma, mean (SD): not reported</p>

Reference	Novick 2018 ³⁵
	<p data-bbox="548 231 1153 263">Injury Severity Score, mean (SD): not reported</p> <p data-bbox="548 343 795 375">Indication for MRI:</p> <ul data-bbox="593 406 1120 678" style="list-style-type: none">• Neck pain, 57.7%• Abnormal neurologic exam, 34.0%• Unable to assess due to:<ul data-bbox="683 510 1120 678" style="list-style-type: none">○ Closed head injury, 17.4%○ Drugs/alcohol, 9.1%○ Post-ictal, 2.1%○ Abnormal CT, 36.5%○ No signs or symptoms, 2.9% <p data-bbox="548 742 1075 774">Setting: secondary care – trauma centre</p> <p data-bbox="548 853 728 885">Country: USA</p> <p data-bbox="548 965 1657 997">Inclusion criteria: underwent both CT and MRI of cervical spine; and history of trauma</p> <p data-bbox="548 1085 952 1117">Exclusion criteria: not reported</p> <p data-bbox="548 1197 1265 1228">People with trauma and suspected cervical spine injury</p>

Reference	Novick 2018³⁵
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury – 17% reported to have closed head injury, but unclear for others if head injury was part of the injury mechanism
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p> <p>Reference standard not reported in the paper but possible to calculate sensitivity of both imaging tests using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>Cervical spine clearance protocol involved clinical confrontational exam for neck pain, neurologic examination and CT of cervical spine. MRI was obtained immediately after CT if neurologic examination was abnormal or if CT indicated an abnormality. If clinical exam identified neck pain or could not be performed, or if the CT interpreted by radiologist as equivocal for abnormality or injury, an MRI was obtained within 48 h of admission.</p> <p>CT images obtained using 1320 or 16-slice machine. Routine trauma protocol consisted of multiple contiguous non-contrast axial sections are obtained from the posterior fossa to the cervical-thoracic junction without the intravenous administration of contrast. Multiplanar reformation was uniformly performed in the coronal and sagittal planes. Screening CT cervical spine slice thickness (acquired at 0.5 mm) with coronal and sagittal reformations was same on both CT scanners with 1-mm cuts and 3-mm reconstruction for coronal and sagittal images.</p> <p>MRI images obtained with 1.5 T magnet, performed in multiple planes and sagittal T1-weighted, T2-weighted, and short-tau inversion-recovery sequences (3 mm thick), as well as an axial T2*-weighted sequence (3 mm thick).</p> <p>Studies assessed as technically adequate if images were obtained from the base of the skull to the first thoracic vertebra and artifact or motion did not markedly limit the evaluation. Studies assessed as not technically adequate by the radiology technician or physician were immediately repeated.</p>

Reference	Novick 2018³⁵				
	Time between measurement of index test and reference standard: CT performed followed by MRI where indicated, duration between the two differed depending on presentation but could be up to 48 h.				
Outcome	Cervical spine injuries – ligamentous or bony injury of the cervical vertebral spine, disc injuries, or spinal cord injuries as assessed by imaging				
2×2 table	Cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	88	NA	88	
	Index test –	13	140	153	
	Total	101	140	241	
	Cervical spine injury – MRI as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	78	NA	78	
	Index test –	23	140	163	
	Total	101	140	241	

Reference	Novick 2018³⁵
Statistical measures	<p>Cervical spinal cord injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 87.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Cervical spinal cord injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 77.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and mean time interval between index test and reference standard likely at least 48 h – applies to both index tests</p> <p>Indirectness: serious – head injury status only clear for 17%, unclear if others had suspected head injury/head imaging</p>
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Parmar 2018³⁶
Study type	Prospective
Study methodology	<p>Data source: clinical audit of single hospital ED. Data obtained from Department of Radiology PACS computer-based database, ICU electronic records and trauma registry.</p> <p>Recruitment: consecutive patients matching inclusion criteria between 9th October 2015 and 8th May 2016 from a single hospital ED</p>
Number of patients	<p>n = 27 analysed</p> <p>(n=100 unconscious patients identified, with n=27 analysed as they had both CT and MRI of cervical spine)</p>
Patient characteristics	<p><u>Note: characteristics only given for n=100 in whole study not the n=27 analysed</u></p> <p>Age, median (IQR): 38.5 (25-53) years</p> <p>Gender (male to female ratio): 81% males</p> <p>Ethnicity: not reported</p> <p>Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p>Mechanism of injury: not reported</p> <p>GCS score at initial trauma, mean (SD): not reported</p>

Reference	Parmar 2018 ³⁶
	<p>Injury Severity Score, median (IQR): 26 (12-33)</p> <p>Setting: secondary care – ED of hospital</p> <p>Country: Australia</p> <p>Inclusion criteria: adults that were unconscious/obtunded and admitted to the ED; and requiring artificial airway and mechanical ventilation – those included in analysis had to have CT and MRI of cervical spine</p> <p>Exclusion criteria: not reported</p> <p>Unconscious/obtunded adults admitted to the ED and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided (assumed to have head injury based on severity of injuries – all obtunded)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p>

Reference	Parmar 2018³⁶				
	<p>MRI reported in paper to be reference standard, but not in line with this review protocol. Therefore, data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>In the study centre, hard neck collar used routinely to immobilise cervical spine until cervical spine injuries can be excluded based on CT scan as primary imaging modality. If no bony injury or malalignment identified on CT, cervical spine is considered radiologically cleared with no further spinal precautions needed. Time-point <48 h used to confirm injury status of cervical spine as benchmark as Australian ICU clearance protocols recommend 48 h or less. Consultant radiologists were on-call and not on-site during off-office ours and were not informed of the audit.</p> <p>Time between measurement of index test and reference standard: unclear duration between CT and MRI.</p>				
Outcome	Any cervical spine injury – poorly defined but includes osseous and ligamentous injuries				
2x2 table	Any cervical spine injury – CT as index test				
		Reference standard +	Reference standard -	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	20	NA	20	
	Index test -	7	0	7	
	Total	27	0	27	
	Any cervical spine injury – MRI as index test				

Reference	Parmar 2018 ³⁶				
		Reference standard +	Reference standard -	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	26	NA	26	
	Index test -	1	0	1	
	Total	27	0	27	
Statistical measures	<p>Any cervical spinal cord injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 74.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Any cervical spinal cord injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 96.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>				
Source of funding	Funding support from WA Health and Raine Medical Research Foundation through Raine Clinical Research Fellowship.				

Reference	Parmar 2018³⁶
Limitations	<p>Risk of bias: very serious – unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and mean time interval between index test and reference standard likely at least 48 h – applies to both index tests</p> <p>Indirectness: serious – all included were obtunded representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p>
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Ptak 2001³⁷
Study type	Retrospective
Study methodology	<p>Data source: retrospective cross-sectional analysis from single general hospital, using radiology report database.</p> <p>Recruitment: retrospective review of those matching inclusion criteria from single general hospital between 1st July 1997 and 31st August 1998.</p>
Number of patients	<p>n = 676</p> <p>(n=2466 cervical spine CT studies identified, of which a subgroup of n=1182 cervical spine studies in trauma patients was selected; within this trauma subgroup, n=676 conforming to screening trauma cervical spine protocol were included)</p>
Patient characteristics	<p>Age, mean (SD): 47.2 (24.1) years, range 1-104 years</p> <p>Gender (male to female ratio): 66.0% males</p>

Reference	Ptak 2001 ³⁷
	<p data-bbox="546 229 835 260">Ethnicity: not reported</p> <p data-bbox="546 347 1747 378">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="546 466 983 496">Mechanism of injury: not reported</p> <p data-bbox="546 584 1229 614">GCS score at initial trauma, mean (SD): not reported</p> <p data-bbox="546 702 1151 732">Injury Severity Score, mean (SD): not reported</p> <p data-bbox="546 820 1294 850">Setting: secondary care – records from a general hospital</p> <p data-bbox="546 938 730 968">Country: USA</p> <p data-bbox="546 1056 2007 1142">Inclusion criteria: presenting to emergency radiology division for CT evaluation of cervical spine injuries following trauma (Massachusetts General Hospital procedure code #644 – having CT of cervical spine); and CT was initial screening evaluation of cervical spine following trauma</p> <p data-bbox="546 1230 2007 1316">Exclusion criteria: non-traumatic injuries; cases where CT was preceded by a plain film series (more than one portable lateral film) of cervical spine; and cases not performed according to standardised ED helical CT protocol for cervical spine screening or those where protocol could not be confirmed</p>

Reference	Ptak 2001³⁷
	People sustaining trauma and suspected cervical spine injury
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>Helical CT of cervical spine</p> <p><u>Reference standard</u></p> <p>Final clinical diagnosis (including operative and discharge notes), possibly incorporating CT results</p> <p>After initial clinical evaluation and portable plain film trauma series including anteroposterior supine chest, pelvis and cross-table lateral view of cervical spine while immobilised in the trauma bay, patients transferred to CT suite. Screening cervical spine images acquired on CT scanner using helical technique with 3 mm beam collimation and pitch of 1.5. Images reconstructed to 3 mm spacing using high spatial frequency bone algorithm. Images acquired from skull base to T2 vertebral body. Images immediately post-processed into 1 mm spacing using detail spatial frequency algorithm, from which 2D coronal and sagittal reformations constructed. Optional 3D reformations available.</p> <p>Time between measurement of index test and reference standard: unclear duration between index tests and other imaging/final diagnosis being confirmed</p>
Outcome	<p>Cervical spine fracture – no further definition provided</p> <p>Positive CT cases for fracture taken as reported in the radiological report.</p>

Reference	Ptak 2001³⁷			
2x2 table	Cervical spine fracture – Helical CT as index test			
		Reference standard +	Reference standard –	Total
	Index test +	59	0	59
	Index test –	1	616	617
	Total	60	616	676
Statistical measures	<p>Cervical spine fracture – Helical CT as index test: reported in paper</p> <p>Sensitivity: 98.3%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 99.8%</p>			
Source of funding	Not reported			
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test, unclear time interval between index test and reference standard and likely that reference standard components differed between patients</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, outcomes focuses only on fractures and unclear if reference standard included a 2 week follow-up period</p>			
Comments	None			

Reference	Raza 2013⁴⁰
Study type	Retrospective
Study methodology	Data source: review of medical records of people presenting to ED of single hospital retrospectively Recruitment: people presenting to ED of single hospital in London between October 2007 and December 2008 retrospectively reviewed
Number of patients	n = 53 (n=108 presenting to ED were reviewed, with n=53 included as they matched inclusion criteria)
Patient characteristics	Age, mean (SD): not reported Gender (male to female ratio): not reported Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: not reported GCS score at initial trauma, mean (SD): not reported

Reference	Raza 2013⁴⁰
	<p>Injury Severity Score, mean (SD): not reported</p> <p>Setting: secondary care – ED of hospital</p> <p>Country: UK</p> <p>Inclusion criteria: adult blunt trauma patients with GCS score ≤ 14 (altered sensorium/obtunded); intoxicated with alcohol or drugs; and cervical spine multidetector CT obtained on admission</p> <p>Exclusion criteria: fracture identified on initial cervical spine multidetector CT; became examinable before additional CS imaging; died before cervical spine clearance; discharge records not available; and those presenting prior to October 2007</p> <p>Adults with altered sensorium/obtunded following blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided (assumed to have head injury based on severity of injuries – all with altered sensorium/obtunded)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p>

Reference	Raza 2013⁴⁰
	<p>Final diagnosis of injury at hospital discharge, follow-up appointments or any readmissions, possibly includes follow-up of at least 2 weeks specified in the protocol given readmissions and follow-up appointments considered</p> <p>PACS and electronic patient records reviewed for patient records and imaging reports in addition to hand search of hospital notes.</p> <p>Time between measurement of index test and reference standard: unclear</p>
Outcome	Clinically significant cervical spine injury – poorly defined
2x2 table	Insufficient reporting of data to be able to calculate 2x2 tables.
Statistical measures	<p>Clinically significant cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 100%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p>
Source of funding	Not reported
Limitations	Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard of final diagnosis includes a period of at least 2 weeks follow-up, reference standard likely not interpreted without knowledge of index test and likely that reference standard different slightly between patients (e.g. any further tests performed)

Reference	Raza 2013⁴⁰
	Indirectness: serious – all included were obtunded/had altered sensorium representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury
Comments	Poor reporting in the paper means specificity is not reported and it is not possible to calculate it.

Reference	Resnick 2014⁴¹
Study type	Prospective
Study methodology	Data source: prospective study of patients from single level 1 trauma centre Recruitment: prospective observational study of consecutive adults matching inclusion criteria between 1 st January 2010 and 31 st May 2011 at single level 1 trauma centre
Number of patients	n = 830 (n=3801 matching inclusion criteria, with n=830 patients requiring imaging as they could not be cleared clinically subsequently included in the analysis)
Patient characteristics	Age, mean (SD): 42.6 (18.0) years Age >55 years, 22.4% Gender (male to female ratio): 70.6% males Ethnicity: not reported

Reference	Resnick 2014 ⁴¹
	<p data-bbox="548 231 1747 263">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="548 343 817 375">Mechanism of injury:</p> <ul data-bbox="593 406 1030 614" style="list-style-type: none">• Motor vehicle collision, 39.8%• Fall, 31.6%• Auto vs. pedestrian, 15.5%• Assault, 8.4%• Motorcycle collision, 4.0%• Other, 0.7% <p data-bbox="548 702 1232 734">GCS score at initial trauma, mean (SD): not reported</p> <p data-bbox="548 821 840 853">Injury severity indices:</p> <ul data-bbox="593 877 1265 1053" style="list-style-type: none">• Injury Severity Score (ISS), mean (SE): 3.3 (2.5)• ISS >25, 0.0%• Chest AIS \geq3, 0.0%• Abdomen AIS \geq3, 0.0%• Extremities AIS \geq3, 0.0% <p data-bbox="548 1141 1064 1173">Setting: secondary care – trauma centre</p> <p data-bbox="548 1260 728 1292">Country: USA</p>

Reference	Resnick 2014⁴¹
	<p>Inclusion criteria: adults (>18 years) sustaining blunt trauma; deemed eligible for evaluation (GCS score 15, not intoxicated and with no distracting injury); underwent CT evaluation of cervical spine; and admitted to centre between 1st January 2010 and 31st May 2011.</p> <p>Exclusion criteria: deemed ineligible for evaluation (GCS score <15; intoxicated; or with a distracting injury)</p> <p>Adults with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p> <p>Final diagnosis at time of discharge (including all imaging and operative findings) – unclear duration of follow-up incorporated into this reference standard</p> <p>Standardised physical examination of cervical spine performed. Collar removed with in-line immobilisation maintained in supine position. Resident or attending surgeon examined for deformities and midline bony tenderness to palpation. Complete peripheral neurologic exam also performed. Those that were awake, alert and able to be examined and had persistent midline pain, tenderness to palpation or focal neurologic deficit enrolled and had CT of cervical spine. MRI was ordered at discretion of attending surgeon or neurosurgeon. All patients monitored on day of discharge.</p>

Reference	Resnick 2014⁴¹																					
	<p>Multidetector-row helical CT performed. Images obtained through occiput to T4. 64-slice scanner variables included no intravenous contrast, 120 kV (p), 100-250 mA, gantry revolution speed 0.5 seconds, beam pitch 0.95 and beam collimation of 64x0.5 mm. Reconstruction performed with 2 mm section thickness in axial, coronal and sagittal planes. Images reviewed in multiple window width and level settings.</p> <p>All MRI scans obtained on 1.5T system, including sagittal T1 fast spin echo (FSE), sagittal T2 FSE, sagittal short tau inversion recovery, axial T2 FSE and axial T1 sequences. Images reviewed at 3 megapixel resolution. Final radiology reading provided by board-certified radiologist used for analysis.</p> <p>(Time between measurement of index test and reference standard: unclear how long between initial CT and final diagnosis at discharge and whether at least 2 weeks as in protocol)</p>																					
Outcome	<p>Any cervical spine injury – any abnormal finding observed on CT or MRI consistent with acute traumatic injury</p> <p>and</p> <p>Clinically significant cervical spine injury – those requiring surgical intervention for stabilisation or halo placement, as well as unstable injuries requiring a hard collar</p>																					
2x2 table	<p>Any cervical spine injury – CT as index test</p> <table border="1" data-bbox="539 1023 2016 1291"> <thead> <tr> <th data-bbox="539 1023 779 1118"></th> <th data-bbox="779 1023 1077 1118">Reference standard +</th> <th data-bbox="1077 1023 1375 1118">Reference standard –</th> <th data-bbox="1375 1023 1615 1118">Total</th> <th data-bbox="1615 1023 2016 1291" rowspan="4">Raw data incompletely reported but missing numbers calculated using excel sheet and sensitivity/specificity values reported in paper</th> </tr> </thead> <tbody> <tr> <td data-bbox="539 1118 779 1182">Index test +</td> <td data-bbox="779 1118 1077 1182">149</td> <td data-bbox="1077 1118 1375 1182">0</td> <td data-bbox="1375 1118 1615 1182">149</td> </tr> <tr> <td data-bbox="539 1182 779 1246">Index test –</td> <td data-bbox="779 1182 1077 1246">15</td> <td data-bbox="1077 1182 1375 1246">666</td> <td data-bbox="1375 1182 1615 1246">681</td> </tr> <tr> <td data-bbox="539 1246 779 1291">Total</td> <td data-bbox="779 1246 1077 1291">164</td> <td data-bbox="1077 1246 1375 1291">666</td> <td data-bbox="1375 1246 1615 1291">830</td> </tr> </tbody> </table>						Reference standard +	Reference standard –	Total	Raw data incompletely reported but missing numbers calculated using excel sheet and sensitivity/specificity values reported in paper	Index test +	149	0	149	Index test –	15	666	681	Total	164	666	830
	Reference standard +	Reference standard –	Total	Raw data incompletely reported but missing numbers calculated using excel sheet and sensitivity/specificity values reported in paper																		
Index test +	149	0	149																			
Index test –	15	666	681																			
Total	164	666	830																			

Reference	Resnick 2014 ⁴¹				
	Clinically significant cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	Raw data incompletely reported but missing numbers calculated using excel sheet and sensitivity/specificity values reported in paper
	Index test +	23	0	23	
	Index test –	0	807	807	
	Total	23	807	830	
Statistical measures	<p>Any cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 90.9%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 97.8%</p> <p>Clinically significant cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 100.0%</p>				

Reference	Resnick 2014⁴¹
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if reference standard of final diagnosis includes a period of at least 2 weeks follow-up, unclear if reference standard interpreted without knowledge of index test and likely that reference standard different slightly between patients(e.g. any further tests performed)</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard incorporates 2 week follow-up period specified in the protocol</p>
Comments	None

Reference	Schoenfeld 2018⁴²
Study type	Retrospective
Study methodology	<p>Data source: obtained from Partners Health System Research Patient Data Registry which gathers clinical data, demographics, radiology results and operative reports on all patients treated at Brigham and Women’s Hospital and Massachusetts General Hospital – two academic level 1 trauma centres</p> <p>Recruitment: retrospectively reviewed database containing data from two level 1 trauma centres between 2007 and 2014</p>
Number of patients	<p>n = 668</p> <p>(n=8753 deemed eligible, with n=8060 having CT of cervical spine and n=693 having both CT and MRI of cervical spine; number analysed further reduced to n=668 for those with CT and MRI based on propensity matching process)</p>
Patient characteristics	Age, mean (SD): 52.6 (22.7) years in CT group and 54.8 (21.7) years in CT-MRI group

Reference	Schoenfeld 2018 ⁴²
	<p data-bbox="546 229 1225 260">Gender (male to female ratio): 60.0% in both groups</p> <p data-bbox="546 346 1397 376">Ethnicity: 72% white in CT group and 76% white in CT-MRI group</p> <p data-bbox="546 462 1747 493">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="546 579 983 609">Mechanism of injury: not reported</p> <p data-bbox="546 695 1391 726">GCS score at initial trauma, mean (SD): 13.3 (3.6) in both groups</p> <p data-bbox="546 812 1659 842">Injury Severity Score, mean (SD): 6.0 (9.7) in CT group and 6.2 (9.4) in CT-MRI group</p> <p data-bbox="546 928 1084 959">Setting: secondary care – trauma centres</p> <p data-bbox="546 1045 730 1075">Country: USA</p> <p data-bbox="546 1161 1960 1222">Inclusion criteria: adults receiving CT alone or CT-MRI for primary evaluation of cervical spine injury following trauma between 2007 and 2014</p>

Reference	Schoenfeld 2018⁴²
	<p>Exclusion criteria: patients with initial evaluations at outside centres that were transferred for care; prior history of spine surgery or spinal metastases; penetrating trauma; those without clear history of trauma despite cervical spine imaging ordered for other reasons; and those lacking complete radiologist reports, emergency room evaluation and/or surgical reports</p> <p>Adults following trauma with suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p> <p>No specific reference standard reported in but data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>CT performed using 128-slice scanner with reference mAs of 180 and 2 mm slice thickness. MRI performed with 1.5 T scanners with axial and sagittal sequences. Imaging results recorded directly from radiologist reports and injury characteristics taken from clinical notes and operative reports.</p> <p>Time between measurement of index test and reference standard: unclear duration between CT and MRI</p>
Outcome	Cervical spine injury – poorly defined

Reference	Schoenfeld 2018 ⁴²				
	Cervical spine injury (for example) fracture, dislocation, traumatic disc herniation and ligamentous disruption on MRI) with associated change in clinical management or surgical intervention was used as primary outcome.				
2x2 table	Cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated. Of the 53 with injury on MRI but not CT, a change of management occurred as a result in n=47 (surgery n=5 and non-operative n=42)
	Index test +	195	NA	195	
	Index test –	53	420	473	
	Total	248	420	668	
	Cervical spine injury – MRI as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	248	NA	248	
	Index test –	0	420	420	
	Total	248	420	668	

Reference	Schoenfeld 2018 ⁴²
Statistical measures	<p>Cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 79.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Cervical spine injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 100.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>
Source of funding	No funding reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and time interval between index test and reference standard unclear – applies to both index tests</p> <p>Indirectness: serious – head injury not mentioned and unclear if all or most had head injury</p>
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Songur 2020⁴⁴
Study type	Retrospective
Study methodology	Data source: cross-sectional study using data from a single ED department at tertiary healthcare centre. Data obtained from hospital electronic medical records. Recruitment: retrospective inclusion from a single centre between June 2014 and June 2018
Number of patients	n = 195 for any injury and n=88 for unstable injuries (n=14,795 with relevant injury codes identified, with n=57 excluded based on a coding error; n=198 identified as having both CT and MRI of the cervical spine, with n=3 of these excluded due to missing data and leaving n=195 for the 'any injury' analysis)
Patient characteristics	Age, mean (SD): 47.34 (21.90) years Gender (male to female ratio): 71.8% males Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: <ul style="list-style-type: none"> • Fall from height, 51.3% • Motor vehicle accident, 33.3% • Pedestrian, 8.7% • Assault, 2.6% • Other mechanism, 4.1%

Reference	<p>Songur 2020⁴⁴</p> <ul style="list-style-type: none"> Unknown, 1.5% <p>GCS score at initial trauma, mean (SD): 97.9% had GCS score >13 and were alert</p> <p>Injury Severity Score, mean (SD): not reported</p> <p>Setting: secondary care – ED department</p> <p>Country: Turkey</p> <p>Inclusion criteria: ICD-10 codes S17 (crushing injury of the neck) or S12 (fracture of cervical vertebra and other parts of the neck); and underwent CT scan followed by MRI within 48 h of admission</p> <p>Exclusion criteria: other diagnoses (coding error); non-diagnostic CT results and/or incomplete medical records</p> <p>People with trauma to the neck and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p>

Reference	Songur 2020 ⁴⁴
	<p><u>Reference standard</u></p> <p>MRI reported in paper to be reference standard, but not in line with this review protocol. Therefore, data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>CT scans performed with GE Discovery HD 750 machine. MRI performed either either 1.5 Tesla Siemens Symphony or 3 Tesla Siemens Avanto CMR scanner. All images assessed by emergency medicine specialist, a neuroradiologist and a neurosurgeon to classify interpretations as ‘negative’ or ‘positive’ for acute traumatic injury patients. CT was positive if impressions included any of the following features: major fractures of vertebrae, disc space widening, vertebral subluxation, epidural hematoma, and prevertebral or paravertebral oedema/hematoma. MRI was positive if they had any of the following features: ligamentous injury, posttraumatic spinal cord pathological signal changes or haemorrhage, epidural/subdural hematoma, new or acute disc herniation and prevertebral oedema or haematoma. MRI that were unequivocally negative for aforementioned findings were classified as MRI-negative.</p> <p>Time between measurement of index test and reference standard: CT scan followed by MRI within 48 h of admission.</p>
<p>Outcome</p>	<p>All cervical spine injuries</p> <p>And</p> <p>Unstable cervical spine injury – based on neurological status of the patient, degree of spinal canal stenosis and degree of instability. Denis’ 1983 definition of single-level ligamentous injury extending to two of three columns.</p>

Reference	Songur 2020 ⁴⁴				
2x2 table	Any cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	64	NA	64	
	Index test –	20	111	131	
	Total	84	111	195	
	Any cervical spine injury – MRI as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	83	NA	83	
	Index test –	1	111	112	
	Total	84	111	195	
	Unstable cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	63	NA	63	
Index test –	18	7	25		
Total	81	7	88		

Reference	Songur 2020 ⁴⁴				
	Unstable cervical spine injury – MRI as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated.
	Index test +	81	NA	81	
	Index test –	0	7	7	
	Total	81	7	88	
Statistical measures	<p>Any cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 76.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Any cervical spine injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 99.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>				

Reference	Songur 2020⁴⁴
	<p>Unstable cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 78.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Unstable cervical spine injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 100.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>
Source of funding	Stated that no financial support was received.
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and time interval between index test and reference standard unclear. In addition, for unstable injuries, fewer participants are analysed compared to any injury and unclear why – applies to both index tests</p> <p>Indirectness: serious – head injury not mentioned and unclear if all or most had head injury</p>
Comments	Not possible to calculate specificity based on the reference standard used.

Reference	Takami 2014⁴⁶
Study type	Prospective
Study methodology	Data source: data prospectively collected from people at single emergency outpatient service Recruitment: prospective collection people transported to emergency outpatient services at single university from September 2007 to May 2009
Number of patients	n = 179 (n=179 identified as matching inclusion criteria and n=179 analysed – no further details about exclusion reasons)
Patient characteristics	Age, average (range): 54.3 (4-94) years Gender (male to female ratio): 74.9% Ethnicity: not reported Head injury: of n=54 with spinal fractures, n=8 had head trauma (intracranial haemorrhage or cranial or facial feature), unclear proportion of whole group Mechanism of injury: not reported

Reference	Takami 2014⁴⁶
	<p>GCS score at initial trauma, mean (SD): not reported</p> <p>Injury Severity Score, average (range): for n=54 with spinal fractures, this was 20.2 (4-70)</p> <p>Setting: secondary care – emergency outpatient service</p> <p>Country: Japan</p> <p>Inclusion criteria: sustained high-energy trauma as determined by emergency personnel on-site and immobilised on a backboard and transported to emergency outpatient services by an ambulance or air ambulance</p> <p>Exclusion criteria: not reported</p> <p>People with high-energy trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – proportion had concomitant head injury but unclear how many, reported to be 15% in those with fractures
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p><u>Reference standard</u></p>

Reference	Takami 2014⁴⁶				
	Full CT of spine				
	Full spine CT performed on same day as arrival. Effective dose of full spine CT calculated in a person with standard body weight. 3D reconstructed image produced using multi-planar construction and presence/absence of fractures determined by two orthopaedic specialists. Plain X-rays of cervical spine examined for all during primary care.				
	Time between measurement of index test and reference standard: unclear but during same admission, possible that reference standard performed prior to index test				
Outcome	Cervical spine fracture – no further definition provided				
2x2 table	Cervical spine fracture – X-ray as index test				
		Reference standard +	Reference standard –	Total	Raw data only sufficient to calculate sensitivity
	Index test +	10	NR	NR	
	Index test –	6	NR	NR	
	Total	16	163	179	
Statistical measures	Cervical spine fracture – X-ray as index test: calculated using excel sheet				
	Sensitivity: 63.0%				
	Specificity: NR				
	PPV: NR				

Reference	Takami 2014⁴⁶
	NPV: NR
Source of funding	Reported that no benefits or funding was received to support this study.
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard and index test were interpreted without knowledge of the other and unclear time interval between index test and reference standard</p> <p>Indirectness: very serious – head injury mentioned for a small proportion of participants but unclear if head injury was part of the injury mechanism for all or most, and outcome focuses specifically on fractures rather than any cervical spine injury</p>
Comments	Only provides sufficient data to calculate sensitivity and not specificity

Reference	Tan 2014⁴⁷
Study type	Retrospective
Study methodology	<p>Data source: electronic medical record database at a single university medical centre</p> <p>Recruitment: retrospective review of records for those matching inclusion criteria at a single medical centre between January 2008 and December 2010</p>
Number of patients	<p>n = 83</p> <p>(n=83 identified as matching inclusion criteria and n=83 analysed – no further details about exclusion reasons)</p>
Patient characteristics	Age, mean (SD): not reported

Reference	Tan 2014 ⁴⁷
	<p data-bbox="546 284 1106 320">Gender (male to female ratio): not reported</p> <p data-bbox="546 400 835 437">Ethnicity: not reported</p> <p data-bbox="546 517 1144 553">Head injury: all had head injury to be included</p> <p data-bbox="546 633 985 670">Mechanism of injury: not reported</p> <p data-bbox="546 750 873 786">GCS score, mean: 12.09</p> <ul data-bbox="595 810 972 879" style="list-style-type: none"><li data-bbox="595 810 954 847">• GCS score 3-10, 24.0%<li data-bbox="595 847 972 879">• GCS score 11-14, 76.0% <p data-bbox="546 959 1153 995">Injury Severity Score, mean (SD): not reported</p> <p data-bbox="546 1075 1576 1112">Setting: secondary care – university medical centre including those with trauma</p> <p data-bbox="546 1192 730 1228">Country: USA</p>

Reference	Tan 2014⁴⁷
	<p>Inclusion criteria: obtunded patients admitted to centre with diagnosis of intracranial haemorrhage and concomitant history of minor cervical spine trauma; and had both CT and MRI of cervical spine</p> <p>Exclusion criteria: not reported</p> <p>People with confirmed intracranial haemorrhage and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – all had head injury to be included
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p> <p>MRI reported in paper to be reference standard, but not in line with this review protocol. Therefore, data available used to calculate sensitivity of CT and MRI using CT + MRI as combined reference standard. This means specificity could not be calculated.</p> <p>CT performed using Siemens 64-slice machine and MRI using Siemens 1.5T or 3T. Both read by board-certified attending neuroradiologist and an attending neurosurgeon.</p> <p>Time between measurement of index test and reference standard: unclear duration between CT and MRI</p>

Reference	Tan 2014⁴⁷				
Outcome	Any cervical spine injury – no definition and Unstable cervical spine injury – no definition				
2×2 table	Any cervical spine injury – CT as index test				
		Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning specificity could not be calculated. All of those with missed injuries on CT scan had intermedullary T2 hyper intensity consistent with possible central cord syndrome, described as not being unstable.
	Index test +	28	NA	28	
	Index test –	4	51	55	
	Total	32	51	83	
	Any cervical spine injury – MRI as index test				
	Reference standard +	Reference standard –	Total	Note false positives were not possible using CT + MRI as a reference standard meaning	
Index test +	32	NA	32		

Reference	Tan 2014 ⁴⁷				
	Index test –	0	51	51	specificity could not be calculated.
	Total	32	51	83	
Statistical measures	<p>Any cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 76.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Any cervical spine injury – MRI as index test: calculated using excel sheet</p> <p>Sensitivity: 99.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p> <p>Unstable cervical spine injury – CT as index test: determined using statements in paper as exact numbers with unstable injuries not provided</p> <p>Sensitivity: 100.0</p> <p>Specificity: NA</p>				

Reference	Tan 2014⁴⁷
	<p>PPV: NA</p> <p>NPV: NA</p> <p>Unstable cervical spine injury – MRI as index test: determined using statements in paper and the fact that sensitivity was 100% for any injuries as exact numbers with unstable injuries not provided</p> <p>Sensitivity: 100.0</p> <p>Specificity: NA</p> <p>PPV: NA</p> <p>NPV: NA</p>
Source of funding	Stated that there was no funding
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unlikely that index test (for MRI) or reference standard (for CT) were interpreted without knowledge of reference standard/index test, and time interval between index test and reference standard unclear = applies to both index tests</p> <p>Indirectness: serious – all included were obtunded representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p>
Comments	Not possible to calculate specificity based on the reference standard used. Unstable injuries described but numbers not given to complete 2x2 tables.

Reference	Vanguri 2014⁴⁸
Study type	Retrospective

Reference	Vanguri 2014⁴⁸
Study methodology	Data source: retrospective review of data from single level 1 trauma centre Recruitment: retrospective inclusion from single level 1 trauma centre between January 2008 and December 2012
Number of patients	n = 5676 (n=5676 identified as matching inclusion criteria and n=5676 analysed – no further details about exclusion reasons)
Patient characteristics	Age, median (range): 39.0 (18-103) years Gender (male to female ratio): not reported Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: not reported GCS score median (range): 15 (3-15) Injury Severity Score, median (range): 5 (1-75)

Reference	Vanguri 2014⁴⁸
	<p>Duration of stay, median (range): 2 (1-175) days</p> <p>Setting: secondary care – trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: adults with blunt trauma; meeting triage criteria for trauma team activation (included vital signs such as GCS, obvious anatomic injury and mechanism); and underwent CT of cervical spine</p> <p>Exclusion criteria: not reported</p> <p>Adults with blunt trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p> <p>Unclear, possibly including other imaging such as MRI and flexion-extension depending on patient</p>

Reference	Vanguri 2014⁴⁸																			
	<p>Siemens Sensation 16 mm multidetector CT used for all patients. Standard protocol included 2 mm thick axial cuts performed at 2 mm increments with sagittal multiplanar reformatted images. Scan extended from base of skull to level of third thoracic vertebra. Findings suggesting ligamentous injury included increased space between ligamentous columns or other contiguous structures, prevertebral haematoma or oedema and abnormal alignment of vertebra. For MRIs, Siemens Avanto 1.5 used, with protocol including 3 mm thick sagittal cuts and 3 mm thick axial cuts with 0.3 mm standard of error. For all imaging only the final attending radiologist reads of scans were considered to determine pathology.</p> <p>Time between measurement of index test and reference standard: unclear at what time-point reference standard was performed/confirmed and how long since initial index test this was</p>																			
Outcome	Cervical spine injury – poorly defined																			
2x2 table	<p>Cervical spine injury – CT as index test</p> <table border="1" data-bbox="539 678 1608 1002"> <thead> <tr> <th data-bbox="539 678 779 767"></th> <th data-bbox="779 678 1072 767">Reference standard +</th> <th data-bbox="1072 678 1373 767">Reference standard –</th> <th data-bbox="1373 678 1608 767">Total</th> </tr> </thead> <tbody> <tr> <td data-bbox="539 767 779 831">Index test +</td> <td data-bbox="779 767 1072 831">420</td> <td data-bbox="1072 767 1373 831">0</td> <td data-bbox="1373 767 1608 831">420</td> </tr> <tr> <td data-bbox="539 831 779 895">Index test –</td> <td data-bbox="779 831 1072 895">0</td> <td data-bbox="1072 831 1373 895">5256</td> <td data-bbox="1373 831 1608 895">5256</td> </tr> <tr> <td data-bbox="539 895 779 1002">Total</td> <td data-bbox="779 895 1072 1002">420</td> <td data-bbox="1072 895 1373 1002">5256</td> <td data-bbox="1373 895 1608 1002">5676</td> </tr> </tbody> </table>					Reference standard +	Reference standard –	Total	Index test +	420	0	420	Index test –	0	5256	5256	Total	420	5256	5676
	Reference standard +	Reference standard –	Total																	
Index test +	420	0	420																	
Index test –	0	5256	5256																	
Total	420	5256	5676																	
Statistical measures	<p>Cervical spine injury – CT as index test: calculated using excel sheet</p> <p>Sensitivity: 1.00</p> <p>Specificity: 1.00</p> <p>PPV: 1.00</p> <p>NPV: 1.00</p>																			

Reference	Vanguri 2014⁴⁸
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if index test and reference standard were interpreted without knowledge of the other, reference standard poorly described and unclear if appropriate, unclear time interval between index test and references standard and possible that not all patients received the same reference standard</p> <p>Indirectness: very serious – head injury not mentioned and unclear if all or most had head injury, and unclear if reference standard included a 2 week follow-up period</p>
Comments	Reference standard poorly described

Reference	Widder 2004⁴⁹
Study type	Prospective
Study methodology	<p>Data source: prospective collection of data from those presenting to a single centre</p> <p>Recruitment: 3-year convenience sample used obtained prospectively presenting to single centre between July 1999 and July 2002</p>
Number of patients	<p>n = 102</p> <p>(n=113 met inclusion criteria, with n=11 excluded as they have incomplete plain film series; leaving n=102 included in the analysis)</p>
Patient characteristics	<p><u>Note: characteristics given only for n=113 matching inclusion criteria and not the n=102 analysed</u></p> <p>Age, average: 35.0 years</p>

Reference	Widder 2004 ⁴⁹
	<p data-bbox="546 229 1120 260">Gender (male to female ratio): 77.0% males</p> <p data-bbox="546 347 835 378">Ethnicity: not reported</p> <p data-bbox="546 466 1747 496">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="546 584 983 614">Mechanism of injury: not reported</p> <p data-bbox="546 702 873 732">GCS score, average: 7.8</p> <p data-bbox="546 820 1016 850">Injury Severity Score, average: 33.2</p> <p data-bbox="546 938 1218 968">Setting: secondary care – those with severe injuries</p> <p data-bbox="546 1056 770 1086">Country: Canada</p> <p data-bbox="546 1174 1984 1235">Inclusion criteria: ≥ 16 years; ISS ≥ 16; GCS score < 9 or intubated with motor score ≤ 5 at presentation to trauma centre and at 24 h – high-risk subpopulation of severely injured patients</p>

Reference	Widder 2004⁴⁹
	<p>Exclusion criteria: diagnosis of cervical cord injury or cervical spine injury at admission; and death within 72 h of arrival at trauma centre</p> <p>Adults with trauma and suspected cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if all or most had head injury as no details provided (assumed to have head injury based on severity of injuries – high risk subpopulation of those severely injured)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine (data not included further in review as not relevant as initial imaging in severely injured)</p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p> <p>For X-ray: CT used as reference standard</p> <p>For CT: final diagnosis at discharge and any readmissions used as reference standard – time-point not mentioned but including readmissions suggests likely >2 weeks (not just limiting to discharge diagnosis)</p> <p>Radiological evaluation consisted of three-view (anteroposterior, lateral and odontoid) cervical spine radiographs. If inadequate films, further views (swimmer’s) were taken. Helical CT then performed (3 mm cuts) from skull base to T1. Axial images and sagittal and coronal reconstruction reviewed. Concomitantly taken to CT scanner for scans of head and other injured areas. Images obtained using 2.5 mm thickness cuts with 3.75 mm rotations. Blinded radiology review of all plain radiographs and CT images performed separately by two independent radiologists. One radiologist reviewed CT scans and the other reviewed plain films. Blinded reviews performed at least 3 months following admission. Complete plain films adequate if all levels visualised including odontoid and C7-T1.</p>

Reference	Widder 2004⁴⁹				
	<p>Clinical follow-up performed using trauma quality improvement process. All initially admitted to ICU. Once weaned from mechanical ventilation, transferred to one of two acute care services (trauma or neurosurgery). Weekly reviews performed to document missed injuries and complications. All charts reviewed at discharge by trauma service registrars to document all injuries. After discharge, patients referred to trauma clinic and/or brain injury clinic for follow-up. Clinics routinely refer missed injuries back to trauma services for review.</p> <p>Time between measurement of index test and reference standard: unclear time interval between tests and follow-up duration for CT reference standard of final diagnosis/readmissions</p>				
Outcome	Cervical spine abnormality – poorly defined				
2×2 table	Cervical spine abnormality – X-ray as index test (CT as reference standard)				
		Reference standard +	Reference standard –	Total	
	Index test +	7	2	9	
	Index test –	11	82	93	
	Total	18	84	102	
	Cervical spine abnormality – CT as index test (final diagnosis at discharge/readmissions as reference standard)				
		Reference standard +	Reference standard –	Total	Does not report raw data to calculate specificity or report specificity in the paper.
	Index test +	18	NR	NR	
	Index test –	0	NR	NR	

Reference	Widder 2004⁴⁹			
	Total	18	84	102
Statistical measures	<p>Cervical spine abnormality – X-ray as index test (CT as reference standard): reported in paper (apart from PPV and NPV which were calculated using excel sheet)</p> <p>Sensitivity: 39.0%</p> <p>Specificity: 98.0%</p> <p>PPV: 78.0%</p> <p>NPV: 88.0%</p> <p>Cervical spine abnormality – CT as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: NR</p> <p>PPV: NR</p> <p>NPV: NR</p>			
Source of funding	Not reported			
Limitations	Risk of bias: serious – unclear if consecutive sample enrolled and some concerns about exclusion criteria, and unclear duration between index test and reference standard – applies to both index tests. In addition, for CT as an index test the reference standard may have different in components between patients.			

Reference	Widder 2004⁴⁹
	Indirectness: serious – all included were within a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury
Comments	None

D.2 Children

Reference	Al-Sarheed 2020²
Study type	Retrospective cohort study
Study methodology	Data source: retrieved data from trauma registry (medical records files from January 2005 to March 2015 and hospital's electronic system from April 2015 to July 2018). Recruitment: retrospective review of patients between January 2005 and July 2018 at King Abdulaziz Medical City, Saudi Arabia. Level 1 trauma centre serving national guard military staff, employees and their families.
Number of patients	n = 62 (n=65 based on raw data reported) (N=62 said to meet inclusion criteria, though this appeared to be n=65 based on raw data reported – no further details about exclusion reasons provided)
Patient characteristics	Age, mean (SD): 8 (3.9) years, range 6 months to 15 years Gender (male to female ratio): 48:14 (77.4% male) Ethnicity: not reported

Reference	Al-Sarheed 2020 ²
	<p data-bbox="546 288 1995 384">Head injury: unclear if all or most suffered concomitant injury to the head. 17.4% with confirmed intra-axial/extra-axial brain haemorrhage, 5.33% with skull/face laceration, 4.33% with brain oedema, 3.88% with brain injury, 3.39% with brain herniation and 23.30% with skull fracture, of those that had associated injuries.</p> <p data-bbox="546 475 712 499">Arrived from:</p> <ul data-bbox="595 533 972 624" style="list-style-type: none"><li data-bbox="595 533 824 560">• Scene, 82.3%<li data-bbox="595 592 972 619">• Referring hospital, 17.7% <p data-bbox="546 710 815 734">Mechanism of injury:</p> <ul data-bbox="595 767 1032 978" style="list-style-type: none"><li data-bbox="595 767 790 794">• Fall, 14.5%<li data-bbox="595 826 1032 853">• Motor vehicle accident, 59.7%<li data-bbox="595 885 882 912">• Pedestrian, 21.0%<li data-bbox="595 944 815 971">• Others, 4.8% <p data-bbox="546 1066 689 1090">Injury type:</p> <ul data-bbox="595 1123 875 1214" style="list-style-type: none"><li data-bbox="595 1123 808 1150">• Blunt, 98.4%<li data-bbox="595 1182 875 1209">• Penetrating, 1.6%

Reference	Al-Sarheed 2020 ²
	<p data-bbox="548 229 1182 261">GCS score at initial trauma, mean (SD): 7.6 (3.7)</p> <p data-bbox="548 347 1171 379">Injury Severity Score, mean (range): 24.1 (0-68)</p> <p data-bbox="548 466 920 497">Duration of stay, mean (SD):</p> <ul data-bbox="595 523 943 616" style="list-style-type: none"><li data-bbox="595 523 920 555">• ICU, 18.2 (36.9) days<li data-bbox="595 580 943 612">• Ward, 29.2 (45.8) days <p data-bbox="548 699 1088 730">Setting: arrived at emergency department</p> <p data-bbox="548 817 837 849">Country: Saudi Arabia</p> <p data-bbox="548 932 1980 1027">Inclusion criteria: aged ≤ 15 years; sustained trauma (motor vehicle accident, fall, struck by falling heavy object, pedestrian, all-terrain vehicle accident and sports injuries); and were intubated at scene or in emergency department.</p> <p data-bbox="548 1114 1585 1145">Exclusion criteria: patients that were awake or were extubated before clearance.</p> <p data-bbox="548 1232 1995 1295">Paediatric patients with suspected cervical spine injury. Reports separately for children < 8 and ≥ 8 years, but not relevant for this review protocol.</p>

Reference	Al-Sarheed 2020²				
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury (assumed to have head injury based on the severity of injuries – all intubated/unconscious)				
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT – institution’s protocol for clearance of cervical spine in obtunded paediatric trauma patient is to perform CT of cervical spine for all patients. MRI considered if there are any abnormal findings on CT scan, significant mechanism of injury or high clinical suspicion.</p> <p><u>Reference standard</u></p> <p>Radiology/clinical examination, including MRI for some where performed. Cases where CT detected cervical spine injury requiring stabilisation were ‘true positives’. Those where CT scan failed to detect cervical spine injury in those that were cervically cleared were classified ‘true negatives’. False negatives were those where CT was negative but patients had evidence of cervical spine injuries either clinically or radiologically. False positives were those with abnormal radiological findings but who were cervically cleared by examination/radiology.</p> <p>Time between measurement of index test and reference standard: for those that had MRI, mean (SD) time from CT to MRI was 5.1 (5.7) days (not all had MRI).</p>				
Outcome	Cervical spine injury mandating stabilisation – no further details provided				
2x2 table	CT vs. radiology/clinical examination – cervical spine injury mandating stabilisation				
		Reference standard +	Reference standard –	Total	Note: numbers given do not match those said to be included (n=62)
	Index test +	28	0	28	
	Index test –	5	32	37	

Reference	Al-Sarheed 2020²			
	Total	33	32	65
Statistical measures	<p><u>CT scan</u></p> <p>Sensitivity: 84.8% (95% CI 68.1-94.8%) – reported in paper</p> <p>Specificity: 100.0% (95% CI 89.1-100.0%) – reported in paper</p> <p>PPV: 100.0 (calculated using spreadsheet)</p> <p>NPV: 86.49 (calculated using spreadsheet)</p>			
Source of funding	Not reported			
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, reference standard likely not interpreted without knowledge of index test and index test may have affected extent of testing/examination used as reference standard, not all had the same reference standard and unclear duration between index test and final diagnosis used as reference standard</p> <p>Indirectness: very serious – all included were unconscious and intubated representing a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury, and unclear if the reference standard matches protocol as definition provided is limited to 'radiology/clinical examination'</p>			
Comments	None			
Reference	Brockmeyer 2012⁵			
Study type	Prospective			

Reference	Brockmeyer 2012 ⁵
Study methodology	Data source: prospective study from single centre Recruitment: prospective enrolment of patients in continuous fashion between November 2005 and September 2009
Number of patients	n = 24 (n=24 enrolled in the study and no details about exclusion reasons provided)
Patient characteristics	Age, range: 4 months to 16 years Gender (male to female ratio): 66.7% males Ethnicity: not reported Head injury: no details reported, unclear if all or most suffered concomitant injury to the head Mechanism of injury: <ul data-bbox="593 1082 943 1286" style="list-style-type: none">• Auto/pedestrian, n=2• Fall, n=3• Skiing, n=1• Scooter, n=1• Kicked by a horse, n=1• Snowmobile, n=1

Reference	Brockmeyer 2012 ⁵
	<ul style="list-style-type: none">• Non-accidental trauma, n=6• All terrain vehicle, n=3• Motor vehicle accident, n=4• Auto/bicycle, n=1• Motorcycle, n=1 <p>GCS score at initial trauma, mean (SD): not reported</p> <p>Injury Severity Score, mean (SD): not reported</p> <p>Setting: secondary care – those with severe injuries admitted to ICU</p> <p>Country: USA</p> <p>Inclusion criteria: GCS score ≤ 8 after haemodynamic stabilisation; admitted to ICU; >2 weeks old and <17 years; and suspected or known traumatic cervical spine injury</p> <p>Exclusion criteria: inability to obtain plain radiographs, CT or MR imaging within 7 days of admission (later amended to 10 days); inability to obtain follow-up plain cervical spine radiographs 3-4 months after injury; and isolated gunshot or penetrating wound to head with little chance of cervical spine injury.</p> <p>Children with severe injury admitted to ICU with suspected cervical spine injury</p>

Reference	Brockmeyer 2012⁵
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury (assumed to have head injury based on severity of injuries – all severely injured and admitted to ICU)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p>CT of cervical spine</p> <p>MRI of cervical spine</p> <p><u>Reference standard</u></p> <p>Clinical outcome/diagnosis of early instability – undergoing surgical correction. Unclear how confirmed but possibly mixture of all available data. Follow-up possibly >2 weeks as mentions plain radiographs at follow-up of 3-4 months post-injury.</p> <p>For each patient a plain lateral cervical spine radiograph, complete cervical spine CT with 2D sagittal and coronal reconstructions, cervical spine MRI imaging with T1 and T2 weighted and short tau inversion recovery images and cervical spine flexion/extension films with fluoroscopy were acquired. Follow-up radiographic imaging consisted of plain lateral flexion-extension radiographs at 3-4 months post-injury. All images obtained using passive motion in an awake patient and read by paediatric neuroradiologist.</p> <p>Time between measurement of index test and reference standard: duration between index tests and confirmed diagnosis unclear.</p>
Outcome	Early cervical spine instability – required surgical correction
2x2 table	Early cervical spine instability (surgical correction) – X-ray (plain radiography) as index test

Reference	Brockmeyer 2012 ⁵				
		Reference standard +	Reference standard -	Total	
	Index test +	1	1	2	
	Index test -	0	22	22	
	Total	1	23	24	
	Early cervical spine instability (surgical correction) – CT as index test				
		Reference standard +	Reference standard -	Total	
	Index test +	1	0	1	
	Index test -	0	23	23	
	Total	1	23	24	
	Early cervical spine instability (surgical correction) – MRI as index test				
		Reference standard +	Reference standard -	Total	
	Index test +	1	6	7	
	Index test -	0	17	17	
Total	1	23	24		

Reference	Brockmeyer 2012 ⁵
Statistical measures	<p>Early cervical spine instability (surgical correction) – X-ray (plain radiographs) as index test: calculated using excel sheet as numbers in paper don't quite match those calculated using raw data throughout study</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 96.0%</p> <p>PPV: 50.0%</p> <p>NPV: 100.0%</p> <p>Early cervical spine instability (surgical correction) – CT as index test: calculated using excel sheet as numbers in paper don't quite match those calculated using raw data throughout study</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 100.0%</p> <p>PPV: 100.0%</p> <p>NPV: 100.0%</p> <p>Early cervical spine instability (surgical correction) – MRI as index test: calculated using excel sheet as numbers in paper don't quite match those calculated using raw data throughout study</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 74.0%</p> <p>PPV: 14.0%</p> <p>NPV: 100.0%</p>

Reference	Brockmeyer 2012⁵
Source of funding	Technical fees for MR imaging portion of study funded by a grant from Primary Children's Foundation.
Limitations	<p>Risk of bias: very serious – unclear if index tests were interpreted without knowledge of other tests and whether reference standard interpreted without knowledge of index test, unclear time interval between index test and reference standard and unclear if reference standard components were the same for all patients – applies to all three index tests</p> <p>Indirectness: serious – all included were at within a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury</p>
Comments	None

Reference	Derderian 2019¹²
Study type	Retrospective study
Study methodology	<p>Data source: hospital trauma registry (from children's hospital with level 1 trauma centre) used to identify those matching inclusion criteria. Patients with traumatic brain, spine or multiorgan injury identified and radiology records subsequently reviewed to narrow it down to those that underwent both CT and MRI following injury. Electronic medical records also queried to obtain a list of all children that underwent MRI of the cervical spine, which were cross-referenced with those from the trauma registry.</p> <p>Recruitment: those matching inclusion criteria between January 2001 and November 2015.</p>
Number of patients	<p>n = 221</p> <p>(n=222 trauma patients had both CT and MRI to evaluate the cervical spine, but n=1 was excluded due to major upper thoracic spinal cord transection with extension into the cervical region; leaving n=221 included in the analysis)</p>

Reference	Derderian 2019 ¹²
Patient characteristics	<p>Age, median (IQR): 9 (3-14) years</p> <p>Gender (male to female ratio): 64.7% male and 35.3% female</p> <p>Ethnicity: not reported</p> <p>Head injury: unclear if all or most had concomitant head injury as part of the injury mechanism – 15.8% said to have isolated head injury, with multiorgan injury including 66.5% which may include head injury</p> <p>Mechanism of injury:</p> <ul style="list-style-type: none">• Motor vehicle accident, 30.8%• Non-accidental trauma, 10.9%• Fall, 10.0%• Skiing/snowboarding/sledding, 5.4%• Other sports-related, 17.6%• Other, 8.6% <p>Type of traumatic injury:</p> <ul style="list-style-type: none">• Isolated head injury, 15.8%

Reference	Derderian 2019 ¹²
	<ul style="list-style-type: none">• Isolated spine injury, 17.6%• Multiorgan, 66.5% <p>Treatment of C-spine:</p> <ul style="list-style-type: none">• Cleared prior to or during hospitalisation, 68.8%• Collar at time of discharge, 15.8%• Deceased prior to clearance, 0.4%• Halo, 1.4%• Fusion surgery (with or without halo), 13.6% <p>Intensive care unit admission: 73.8%</p> <p>Intensive care unit length of stay, median (IQR): 8 (3-13) days</p> <p>Hospital length of stay, median (IQR): 15 (4-36) days</p> <p>GCS score score median (IQR): 11 (5-15)</p> <p>Setting: secondary care – trauma patients at children’s hospital</p>

Reference	Derderian 2019¹²
	Country: USA
	Inclusion criteria: children that received CT and MRI of cervical spine following trauma
	Exclusion criteria: one child excluded with a major upper thoracic spinal cord transection with extension into the cervical region.
	Paediatric trauma patients undergoing cervical spine CT and MRI scan
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury
Index test(s) and reference standard	<u>Index test</u> CT – stable or unstable injury on CT used as CT-positive Or MRI – stable or unstable injury on MRI used as MRI-positive <u>Reference standard</u>

Reference	Derderian 2019 ¹²
	<p>Study not specifically reported as a diagnostic accuracy study. Calculated accuracy from data provided for CT and MRI alone in predicting clinical instability (defined as undergoing intervention by halo placement or spinal fusion). Unclear follow-up period covered by the data.</p> <p>Time between measurement of index test and reference standard: unclear time period between CT and MRI, unclear follow-up period in terms of intervention being performed.</p> <p>Institutional protocol was as follows: cervical spine imaging in those with risk factors for cervical spine injury. Those that could cooperate with a clinical examination also had a supplemental 3-view radiograph if >5 years. For those ≤5 years, odontoid view replaced by right and left oblique cervical radiography. CT reserved for those with risk factors who were unable to participate in a clinical examination or had significant distracting injury. If no CT findings of unstable spinal column or a spinal cord injury and the suspicion for one was low, MRI was deferred until the patient demonstrated improved clinical status sufficient for extubation and thorough neurological examination. If this did not occur within 72 h then the MRI was obtained and collar removed if no unstable cervical spine injury observed.</p> <p>Abnormal imaging findings included fracture, translation, angulation, herniated nucleus pulposus, intraspinal haematoma or ligamentous injury. Ligamentous injury considered column-disrupting if normal linear T2 hypointense structure of the anterior longitudinal ligament, posterior longitudinal ligament or ligamentum flavum was interrupted to suggest a complete ligamentous tear. Isolated oedema in interspinous ligaments not considered column-disrupting injury. If any of these abnormalities were not associated with disruption of two or more spinal columns then they were considered stable.</p> <p>Imaging results for CT and MRI categorised into one of three groups: no injury, stable injury and unstable injury.</p>
Outcome	<p>Clinical instability – those undergoing a surgical intervention (spinal fusion or halo placement) were defined as clinically unstable in the study.</p>

Reference	Derderian 2019 ¹²				
2×2 table	CT vs. reference standard (clinical instability – surgical spinal fusion or halo placement)				
		Reference standard +	Reference standard –	Total	Note that these tables and subsequent accuracy results provided under ‘statistical measures’ were calculated from data provided in the paper.
	Index test +	33	28	61	
	Index test –	0	160	160	
	Total	33	188	221	
	MRI vs. reference standard (clinical instability – surgical spinal fusion or halo placement)				
		Reference standard +	Reference standard –	Total	Note that these tables and subsequent accuracy results provided under ‘statistical measures’ were calculated from data provided in the paper.
	Index test +	33	104	137	
	Index test –	0	84	84	
	Total	33	188	221	
Statistical measures	CT vs. reference standard (clinical instability – surgical spinal fusion or halo placement) – calculated from data in paper				
	Sensitivity: 1.00				
	Specificity: 0.85				
	PPV: 0.54				
	NPV: 1.00				

Reference	Derderian 2019¹²
	<p>MRI vs. reference standard (clinical instability – surgical spinal fusion or halo placement) – calculated from data in paper</p> <p>Sensitivity: 1.00</p> <p>Specificity: 0.45</p> <p>PPV: 0.24</p> <p>NPV: 1.00</p>
Source of funding	Reported to be no funding
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, likely that results of index tests affected decisions about considering intervention (reference standard) and unclear duration of follow-up for intervention and whether follow-up was similar for all patients – applies to both index tests</p> <p>Indirectness: serious – unclear if all of the majority also sustained a head injury</p>
Comments	Not formally described as a diagnostic accuracy study and no sensitivity etc. reported, but data available to calculate sensitivity and specificity for clinically unstable injuries.

Reference	Henry 2013-2²⁵
Study type	Retrospective study
Study methodology	Data source: retrospective review of patients treated for cervical spine injury using paediatric trauma database at Tufts Medical Center (level 1 paediatric trauma centre)

Reference	Henry 2013-2²⁵
	Recruitment: retrospective review of database.
Number of patients	n = 84 (n=84 said to match inclusion criteria and n=84 analysed – no details about exclusion reasons)
Patient characteristics	Age, mean (SD): 9.0 (5.8) years Gender (male to female ratio): 56% male and 44% female Ethnicity: not reported Head injury: no mention of head injury, unclear if all or majority had concomitant head injury as part of the injury mechanism. Mechanism of injury: <ul style="list-style-type: none">• Sports/physical activity, 28%• Motor vehicle accident, 32%• Domestic violence, 6%• Fall, 29%• Self-inflicted, 1%

Reference	Henry 2013-2²⁵
	<ul style="list-style-type: none"> • Non-specific/unclear, 4% <p>GCS score, mean (range): 12.8 (3-15)</p> <p>Setting: secondary care – trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: aged ≤18 years at time of injury; involved in a trauma; and had CT and MRI scans of the cervical spine performed within 48 h of injury.</p> <p>Exclusion criteria: not reported.</p> <p>Paediatric patients evaluated for cervical spine injury.</p>
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury
Index test(s) and reference standard	<u>Index test and reference standard</u>

Reference	Henry 2013-2²⁵			
Outcome	<p>CT and MRI were both an index test as well as a reference standard, depending on the type of injury. CT was used as the reference standard for osseous injury (bony injuries – fractures, locked facets, subluxations and dislocations) and MRI was used as the reference standard for soft tissue injuries (compression fractures, soft tissue oedema, ligamentous injury, muscular injury and spinal cord injury).</p> <p>Time between measurement of index test and reference standard: mean (range) time between CT and MRI was 0.4 (0-2) days. 80/84 had CT prior to MRI scan, while 4 had MRI prior to CT scan. Time between injury and CT was 0.3 (0-1) days and between injury and MRI was 0.7 (0-2) days.</p> <ul style="list-style-type: none"> • Osseous injury (reference standard as CT): fractures, locked facets, subluxations and dislocations • Soft tissue injury (reference standard as MRI): compression fractures, soft tissue oedema, ligamentous injury, muscular injury and spinal cord injury 			
2×2 table	MRI vs. CT (reference standard) for osseous injury			
		Reference standard +	Reference standard –	Total
Index test +	6	2	8	
Index test –	0	76	76	
Total	6	78	84	
	CT vs. MRI (reference standard) for soft tissue injury			
		Reference standard +	Reference standard –	Total
Index test +	3	0	3	

Reference	Henry 2013-2²⁵			
	Index test –	10	71	81
	Total	13	71	84
Statistical measures	<p>MRI vs. CT (reference standard) for osseous injury – values reported in paper</p> <p>Sensitivity: 100%</p> <p>Specificity: 97%</p> <p>PPV: 75%</p> <p>NPV: 100%</p> <p>CT vs. MRI (reference standard) for soft tissue injury – values reported in paper</p> <p>Sensitivity: 23%</p> <p>Specificity: 100%</p> <p>PPV: 100%</p> <p>NPV: 88%</p>			
Source of funding	Not reported			
Limitations	Risk of bias: very serious - unclear if consecutive sample enrolled and depending on the type of injury detected (osseous or soft tissue), index or reference standard was likely interpreted with knowledge of the other as CT performed first in most cases – applies to both index tests			

Reference	Henry 2013-2²⁵
	Indirectness: very serious - unclear if all or the majority also sustained a head injury and outcome limited to fractures or ligamentous injury depending on the index test
Comments	None

Reference	Henry 2013-1²⁶
Study type	Retrospective study
Study methodology	Data source: retrospective review of patients treated for cervical spine injury using paediatric trauma database at Tufts Medical Center (level 1 paediatric trauma centre) Recruitment: those between 2002 and 2011 in the database and matching inclusion criteria were included
Number of patients	n = 73 (n=146 meeting inclusion criteria identified, with n=12 excluded due to lack of information about cervical spine clearance in medical charts, n=23 prescribed a rigid collar and cleared at follow-up and n=38 without follow-up information on record excluded; leaving n=73 included in the analysis)
Patient characteristics	Age, mean (SD): 8.3 (5.8) years Gender (male to female ratio): 65% male and 35% female Ethnicity: not reported

Reference	Henry 2013-1 ²⁶
	<p data-bbox="546 288 1995 352">Head injury: no mention of head injury, unclear if all or majority had concomitant head injury as part of the injury mechanism.</p> <p data-bbox="546 440 819 472">Mechanism of injury:</p> <ul data-bbox="595 499 1016 831" style="list-style-type: none"><li data-bbox="595 499 1016 531">• Sports/physical activity, 22%<li data-bbox="595 560 1016 592">• Motor vehicle accident, 40%<li data-bbox="595 620 1016 652">• Domestic violence, 3%<li data-bbox="595 681 1016 713">• Fall, 28%<li data-bbox="595 742 1016 774">• Self-inflicted, 0%<li data-bbox="595 802 1016 834">• Non-specific/unclear, 7% <p data-bbox="546 916 853 948">Indications for imaging:</p> <ul data-bbox="595 975 1016 1307" style="list-style-type: none"><li data-bbox="595 975 1016 1007">• Neck pain, 12%<li data-bbox="595 1035 1016 1067">• Neurological deficit, 3%<li data-bbox="595 1096 1016 1128">• Neurological symptom, 8%<li data-bbox="595 1157 1016 1189">• Distracting injuries, 44%<li data-bbox="595 1217 1016 1249">• Sedation/intubation, 16.5%<li data-bbox="595 1278 1016 1310">• Pain + ≥ 1 other factor, 16.5%

Reference	Henry 2013-1²⁶
	<p>GCS score at admission, mean (SD): 12.1 (5.0)</p> <p>Duration of stay, mean: 4.6 days (range, 0-28 days)</p> <p>Setting: secondary care – paediatric trauma centre</p> <p>Country: USA</p> <p>Inclusion criteria: aged ≤18 years at the time of injury; could not be cleared by means of clinical criteria; and underwent MRI of the cervical spine with a STIR (short T1 inversion recovery) sequence within 48 h of injury.</p> <p>Exclusion criteria: excluded a group that required a hard collar and clearance at follow-up, focusing on those that were cleared prior to discharge (may affect diagnostic accuracy results?); and lack of information about cervical spine clearance in medical charts.</p> <p>Paediatric patients being assessed for cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury
Index test(s) and reference standard	<p><u>Index test</u></p> <p>MRI with STIR sequence</p>

Reference	Henry 2013-1²⁶			
	<p><u>Reference standard</u></p> <p>Follow-up or flexion/extension radiographs – injury requiring surgical intervention or presenting with clinical (significant pain or neurological compromise) or radiographic evidence of instability upon follow-up. Flexion-extension radiographs used to identify false positive findings on MRI. Mean follow-up 10.0 (18.4) months, range 4 days – 7.6 years.</p> <p>MRI diagnosis of cervical injury requiring surgical stabilisation considered true positives and cases where MRI findings were negative and patients cleared as in-patients with follow-up information on record were true negatives (no surgical intervention and no instability or pain at follow-up). False negatives defined as cases where patient displayed clinical (significant pain or neurological compromise) or radiographic evidence of instability during follow-up with an initially negative MRI. False positive defined as case where MRI showed abnormal findings but patient was cleared by flexion-extension radiographs during admission (only used if patient had reasonable range of cervical motion).</p> <p>Time between measurement of index test and reference standard: unclear time between MRI and flexion-extension where this was used, mean follow-up of 10.0 months in terms of cases where follow-up was used as reference standard.</p>			
Outcome	Cervical spine injury – instability: requiring surgical stabilisation – either undergoing it or demonstrating signs of instability, pain or neurological compromise during follow-up).			
2x2 table	MRI STIR vs. reference standard (follow-up with/without flexion-extension radiographs during admission)			
		Reference standard +	Reference standard –	Total
Index test +	1	2	3	

Reference	Henry 2013-1²⁶			
	Index test –	0	70	70
	Total	1	72	73
Statistical measures	<p>MRI STIR vs. reference standard (follow-up with/without flexion-extension radiographs during admission) – reported in paper</p> <p>Sensitivity: 100%</p> <p>Specificity: 97%</p> <p>PPV: 33%</p> <p>NPV: 100%</p>			
Source of funding	Not reported			
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, excluded a group that were discharged in a hard collar and cleared later, unlikely that reference standard was interpreted without knowledge of index test results and reference standard varied between patients</p> <p>Indirectness: serious – unclear if all or the majority also sustained a head injury</p>			
Comments	None			

Reference	Qualls 2015³⁸
Study type	Retrospective cohort study

Reference	Qualls 2015 ³⁸
Study methodology	<p>Data source: trauma registry at St. Louis Children’s Hospital (academic children’s hospital with level 1 trauma certification) queried to identify all patients matching inclusion criteria.</p> <p>Recruitment: those admitted between 1st January 2002 and 31st December 2012.</p>
Number of patients	<p>n = 63</p> <p>(n=64 met inclusion criteria, with n=1 excluded due to a previous cervical spine injury; leaving n=63 included in the analysis)</p>
Patient characteristics	<p>Age, median (range): 9.6 (0.1-17.8) years</p> <p>Gender (male to female ratio): 52.4% male and 47.6% female</p> <p>Ethnicity: not reported</p> <p>Head injury: all had severe traumatic brain injury to be included</p> <p>Mechanism of injury:</p> <ul style="list-style-type: none"> • Motor vehicle occupant, 47.6% • Non-accidental trauma, 20.6% • Other motorised transport crash, 14.3% • Pedestrian vs. automobile, 14.3%

Reference	Qualls 2015 ³⁸
	<ul style="list-style-type: none"><li data-bbox="595 236 965 261">• Fall from elevation, 3.2% <p data-bbox="551 352 913 378">GCS score, median (range):</p> <ul style="list-style-type: none"><li data-bbox="595 411 837 437">• In ED, 5 (3-13)<li data-bbox="595 470 1077 496">• At neurosurgical consult, 6 (3-13)<li data-bbox="595 529 1346 555">• At admission to paediatric intensive care unit, 6 (3-14) <p data-bbox="551 646 1182 671">Injury Severity Score, median (range): 30 (11-75)</p> <p data-bbox="551 762 1234 788">Paediatric trauma score, median (range): 3 (-3 to 10)</p> <p data-bbox="551 879 1189 904">Duration of stay, median (range): 34 (5-129) days</p> <p data-bbox="551 995 1547 1021">Duration of paediatric intensive care unit stay, median (range): 13 (2-34) days</p> <p data-bbox="551 1112 680 1137">Intubated:</p> <ul style="list-style-type: none"><li data-bbox="595 1171 815 1197">• In ED, 90.5%<li data-bbox="595 1230 1055 1256">• At neurosurgical consult, 96.8%<li data-bbox="595 1289 1323 1315">• At admission to paediatric intensive care unit, 98.4%

Reference	Qualls 2015 ³⁸
	<p>Setting: secondary care – trauma injuries admitted to hospital</p> <p>Country: USA</p> <p>Inclusion criteria: severe traumatic brain injury admitted to hospital; and received cervical spine MRI and cervical spine CT.</p> <p>Exclusion criteria: those receiving cervical spine MRI but that had a history of previous cervical spine injury; GCS score >8 at admission to ED, initial neurosurgery evaluation and admission to paediatric intensive care unit (all three time-points) were excluded.</p> <p>Children with severe traumatic brain injury and assessed for cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury in children with severe traumatic brain injury
Index test(s) and reference standard	<p><u>Index test</u></p> <p>CT alone</p> <p>MRI alone</p> <p><u>Reference standard</u></p> <p>CT followed by MRI (CT + MRI)</p>

Reference	Qualls 2015³⁸			
	<p>Presence of injury on CT or MRI determined by review of all imaging reports by a paediatric neurosurgeon and a paediatric emergency physician. They determined whether patients had an injury, whether it was unstable and which imaging modalities were able to detect the injuries seen. Institutional protocol did not require plain radiography of the cervical spine but where this had been performed the imaging was evaluated in the same way as CT and MRI and determined to demonstrate evidence of injury or no evidence of injury.</p> <p>Time between measurement of index test and reference standard: reference standard was the process of using both rather than only a single imaging test. Institutional protocol was to perform MRI if no improvement in mental status or intubation >72 h.</p> <p>Institutional protocol was as follows for patients with significant altered mental status or intubation following blunt trauma: axial cervical spine CT for all children immediately on presentation. Cervical spine precautions continued for those with normal CT. If mental status and intubation normalised within 72 h, children were cleared clinically. Otherwise, MRI obtained if persisted >72 h. If MRI was normal, patients were cleared and cervical spine precautions discontinued.</p>			
Outcome	<ul style="list-style-type: none"> • Unstable cervical spine injury – injury resulting in neurological deficit localised to cervical spinal cord, operative stabilisation, halo placement or cervical immobilisation of 3 months or greater (duration obtained from patient records including follow-up appointments by neurosurgery service). • Any cervical spine injury, including those that were not considered unstable as well as unstable injuries. 			
2x2 table	Unstable cervical spine injury – CT alone vs. CT followed by MRI (reference standard)			
	Reference standard +	Reference standard –	Total	

Reference	Qualls 2015 ³⁸					
	Index test +	5	9	14	Raw data calculated from diagnostic accuracy measures provided in paper.	
	Index test -	0	49	49		
	Total	5	58	63		
	Unstable cervical spine injury – MRI alone vs. CT followed by MRI (reference standard)					
		Reference standard +	Reference standard -	Total	Raw data calculated from diagnostic accuracy measures provided in paper.	
	Index test +	4	11	15		
	Index test -	1	47	48		
	Total	5	58	63		
	Any cervical spine injury – CT alone vs. CT followed by MRI (reference standard)					
	Not possible to calculate raw data from accuracy measures provided as only sensitivity and NPV were reported.					
Any cervical spine injury – MRI alone vs. CT followed by MRI (reference standard)						
Not possible to calculate raw data from accuracy measures provided as only sensitivity and NPV were reported.						
Statistical measures	Unstable cervical spine injury – CT alone vs. CT followed by MRI (reference standard) – as reported in paper Sensitivity: 100% (95% CI 48-100%) Specificity: 84.5% (95% CI 73-93%)					

Reference	Qualls 2015 ³⁸
	<p>PPV: 35.7% (95% CI 13-65%) NPV: 100% (95% CI 93-100%)</p> <p>Unstable cervical spine injury – MRI alone vs. CT followed by MRI (reference standard) – as reported in paper</p> <p>Sensitivity: 80% (95% CI 29% to 97%) Specificity: 81% (95% CI 79-90%) PPV: 26.7% (95% CI 8-55%) NPV: 98% (95% CI 89% to 100%)</p> <p>Any cervical spine injury – CT alone vs. CT followed by MRI (reference standard) – as reported in paper</p> <p>Sensitivity: 63.2% (95% CI 38-84%) Specificity: NR PPV: NR NPV: 86.3% (95% CI 74-94%)</p> <p>Any cervical spine injury – MRI alone vs. CT followed by MRI (reference standard) – as reported in paper</p> <p>Sensitivity: 68.4% (95% CI 43-87%) Specificity: NR</p>

Reference	Qualls 2015³⁸
	PPV: NR NPV: 88% (95% CI 76-95%)
Source of funding	No funding was received for the study
Limitations	Risk of bias: very serious – unclear if consecutive sample enrolled, either index test (for MRI alone) or reference standard (for CT alone) unlikely to have been interpreted without knowledge of the other and appears to be 72 h between CT and MRI being performed – applies to both index tests Indirectness: serious – all included were within a more severely injured subgroup which may be less applicable to general population of those attending ED with suspected cervical spine injury
Comments	2x2 data not reported so calculated from the diagnostic accuracy measures reported (sensitivity etc.)

Reference	Rana 2009³⁹
Study type	Retrospective
Study methodology	Data source: retrospective review of data from single children’s hospital which has level 1 paediatric trauma centre status Recruitment: retrospective review of children from single level 1 trauma centre between 2004 and 2006
Number of patients	n = 54 (n=318 had imaging for cervical spine injury, with n=54 with both CT and plain films included in the analysis)
Patient characteristics	<u>Note: characteristics reported only for n=318 patients identified not specifically those analysed with both CT and MRI (n=54)</u> Age, mean: 10.2 years

Reference	Rana 2009 ³⁹
	<p data-bbox="548 284 1120 320">Gender (male to female ratio): 64.0% males</p> <p data-bbox="548 400 835 437">Ethnicity: not reported</p> <p data-bbox="548 517 1747 553">Head injury: no details reported, unclear if all or most suffered concomitant injury to the head</p> <p data-bbox="548 633 985 670">Mechanism of injury: not reported</p> <p data-bbox="548 750 1039 786">GCS score at initial trauma, mean: 13</p> <p data-bbox="548 866 985 903">Injury Severity Score, mean: 14.2</p> <p data-bbox="548 983 772 1019">Intubated, 24.0%</p> <p data-bbox="548 1099 1395 1136">Setting: secondary care – those with trauma at children’s hospital</p> <p data-bbox="548 1216 730 1252">Country: USA</p>

Reference	Rana 2009³⁹
	<p>Inclusion criteria: paediatric trauma patients (<18 years); and cervical spine imaging and/or a confirmed cervical spine injury</p> <p>Exclusion criteria: those without cervical spine imaging or a cervical spine injury.</p> <p>Children sustaining trauma and with suspected or confirmed cervical spine injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray of cervical spine</p> <p>CT of cervical spine</p> <p><u>Reference standard</u></p> <p>CT used as ‘gold standard’ for X-ray, but clinical outcome used as gold standard for CT, which includes subsequent imaging where performed. Follow-up unclear for reference standard of clinical outcome.</p> <p>Institutional protocol included initial physical examination of cervical spine. Those with reliable exams and who were fully aware without motor/sensory deficits, neck pain, evidence of intoxicating agents and distracting injuries were cleared clinically in the trauma centre. No further evaluation of cervical spine was required (excluded from study). If there were complaints of neck tenderness, neurologic deficits, abnormal GCS or distracting pain from another imaging, cervical spine imaging was performed (plain radiographs, CT or both at discretion of trauma team leader). If radiographs negative for injury, initial stabilisation collar changed to padded collar until reliable examination performed. Flexion and extension views performed in those with continued cervical tenderness or if</p>

Reference	Rana 2009³⁹
	<p>prolonged intubation required. If pain persisted, discharged home with cervical spine collar and followed up by neurosurgery team for clearance.</p> <p>Time between measurement of index test and reference standard: duration between index tests and confirmed diagnosis unclear.</p>
Outcome	Cervical spine injury – poorly defined
2x2 table	Raw data reported difficult to follow in paper (unclear how many analysed for X-ray) and attempts to work out do not match sensitivity/specificity values reported in paper. Values reported in paper therefore used and 2x2 tables not completed.
Statistical measures	<p>Cervical spine injury – X-ray as index test: reported in paper</p> <p>Sensitivity: 61.5%</p> <p>Specificity: 1.6%</p> <p>PPV: 61.5%</p> <p>NPV: NR</p> <p>Cervical spine injury – CT as index test: reported in paper</p> <p>Sensitivity: 100.0%</p> <p>Specificity: 97.6%</p> <p>PPV: 79.4%</p> <p>NPV: NR</p>
Source of funding	Not reported

Reference	Rana 2009³⁹
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if reference standard interpreted without knowledge of index test and unclear interval between index test and reference standard – applies to both index tests. In addition, for CT as an index test, it is possible that the reference standard components differed between patients</p> <p>Indirectness:</p> <p>X-ray as index test – serious - unclear if all or the majority also sustained a head injury</p> <p>CT as index test – very serious - unclear if all or the majority also sustained a head injury, and unclear if follow-up of at least 2 weeks as part of the reference standard</p>
Comments	None

Reference	Somppi 2018⁴³
Study type	Retrospective cohort study
Study methodology	<p>Data source: those matching inclusion criteria and presenting to urban tertiary care centre (designated ACS level 1 paediatric trauma centre). Suspected cervical spine injury identified from radiology database using ICD codes 70490, 70492 and 87.22 of ninth revision. These correspond to cervical CT without contrast, soft tissue cervical CT with and without contrast, and other X-ray of cervical spine. Also reviewed hospital trauma registry for study period to identify those with neck injuries that may have been missed by automated search.</p> <p>Recruitment: those matching inclusion criteria between 1st January 2011 and 31st December 2013 included.</p>

Reference	Somppi 2018 ⁴³
Number of patients	<p>n = 574</p> <p>(n=671 in the base dataset, with n=27 with no cervical spine injury suspected, n=10 with no consent for retrospective studies, n=49 with CT imaging not performed at the institution and n=11 with unavailable records/not admitted to ER excluded; leaving n=574 included in the analysis)</p>
Patient characteristics	<p>Age, median (IQR): 9.70 (4.78-13.83) years</p> <p>Gender (male to female ratio): 57.5% male and 42.5% female</p> <p>Ethnicity: not reported</p> <p>Head injury: unclear proportion that also sustained a head injury, n=230 (40%) underwent head CT</p> <p>Disposition:</p> <ul style="list-style-type: none"> • Discharged, 78.6% • Admitted, 21.4% <p>Mechanism of injury:</p> <ul style="list-style-type: none"> • Fall, 50.0% • Sports, 22.2% • Motor vehicle accident, 12.7%

Reference	Somppi 2018 ⁴³
	<ul style="list-style-type: none">• Other/unknown, 15.0% <p>GCS score: not reported</p> <p>Cervical spine imaging performed:</p> <ul style="list-style-type: none">• X-ray, 86.6%• CT, 47.9%• MRI, 4.9%• Single imaging study, 51.7%• Two imaging studies, 40.9%• Three imaging studies, 6.6%• Four or more imaging studies, 0.5% <p>Setting: secondary care</p> <p>Country: USA</p> <p>Inclusion criteria: children and adolescents (aged ≤19 years); presenting with possible neck injury to urban tertiary care centre</p>

Reference	Somppi 2018⁴³
	<p>Exclusion criteria: underwent CT imaging as part of a diagnostic procedure (i.e. for abscess drainage or interventional radiology); patients receiving CT imaging before transfer to the trauma centre the study was performed at; no cervical spine injury suspected (e.g. imaging performed for fever with neck pain and no related trauma); no consent for retrospective studies; and record unavailable or not admitted to the emergency room.</p> <p>Children and adolescents presenting with possible neck injury</p>
Target condition(s)	Suspected cervical spine injury – unclear if most/all had head injury (40% had head CT)
Index test(s) and reference standard	<p><u>Index test</u></p> <p>X-ray (n=495)</p> <p>CT (n=130)</p> <p>MRI (n=21)</p> <p><u>Reference standard</u></p> <p>Unclear, possibly all imaging and follow-up? To ensure complete identification of spinal cord injuries, medical records for all patients with a negative imaging study (CT or MRI) were reviewed for up to 1 month after the index ED visit to assess for cervical spine pain on ED or outpatient visits to the institution.</p>

Reference	Somppi 2018⁴³
	Time between measurement of index test and reference standard: time between different types of imaging unclear, up to 1 month follow-up for those with negative imaging CT or MRI.
Outcome	Cervical spine injury – ligamentous or osseous injury documented by attending radiologist in their report. Patients with spinal cord injury without radiograph evidence were defined as those with MRI abnormalities indicating spinal cord injury but with a negative X-ray or CT OR any patient re-presenting after initial index ED visit with persistent cervical spine pain or neurologic abnormalities (e.g., tingling, numbness) that then underwent MRI which revealed ligamentous or osseous injuries.
2x2 table	Raw data incompletely reported and could not calculate raw data from diagnostic accuracy measures provided, meaning 2x2 tables could not be completed. A total of 8 patients had confirmed cervical spine injury.
Statistical measures	<p>X-ray vs. reference standard (imaging/follow-up?) – reported in study (n=495)</p> <p>Sensitivity: 0.83 (95% CI 0.36-0.99)</p> <p>Specificity: 0.97 (95% CI 0.96-0.99)</p> <p>PPV: 0.31 (95% CI 0.12-0.59)</p> <p>NPV: 0.99 (95% CI 0.98-0.99)</p> <p>CT vs. reference standard (imaging/follow-up?) – reported in study (n=130)</p> <p>Sensitivity: 1.00 (95% CI 0.52-1.00)</p> <p>Specificity: 1.00 (95% CI 0.96-1.00)</p> <p>PPV: 1.00 (95% CI 0.52-1.00)</p> <p>NPV: 1.00 (95% CI 0.96-1.00)</p>

Reference	Somppi 2018⁴³
	<p>MRI vs. reference standard (imaging/follow-up?) – reported in study (n=21)</p> <p>Sensitivity: 1.00 (95% CI 0.51-1.00)</p> <p>Specificity: 1.00 (95% CI 0.75-1.00)</p> <p>PPV: 1.00 (95% CI 0.52-1.00)</p> <p>NPV: 1.00 (95% CI 0.75-1.00)</p>
Source of funding	Not reported
Limitations	<p>Risk of bias: very serious – unclear if consecutive sample enrolled, unclear if index tests all interpreted without knowledge of reference standard, reference standard used for each index test unclear as is whether reference standard was interpreted without knowledge of index test and unclear time interval between index test and reference standard and whether all received the same reference standard – applies to all three index tests</p> <p>Indirectness: very serious – unclear if all or the majority also sustained a head injury (40% said to have had head CT) and reference standard poorly defined so unclear if matches protocol.</p>
Comments	2x2 data not reported. Attempted to calculate based on diagnostic accuracy measures provided (sensitivity etc.), but numbers were not consistent with the number analysed.

Appendix E – Forest plots

E.1 Coupled sensitivity and specificity forest plots

E.1.1 Adults – all having index test and not limited to those that were admitted

E.1.1.1 X-ray as index test

Figure 2: Those with blunt trauma with all having head CT, CT as reference standard, cervical spine fracture as outcome

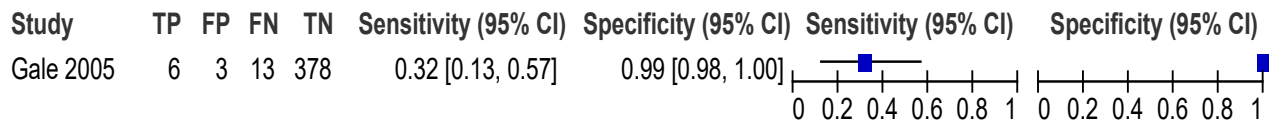


Figure 3: Those with trauma and low risk (one NEXUS criterion), unclear if head injury, CT as reference standard, clinically significant cervical spine injury as outcome

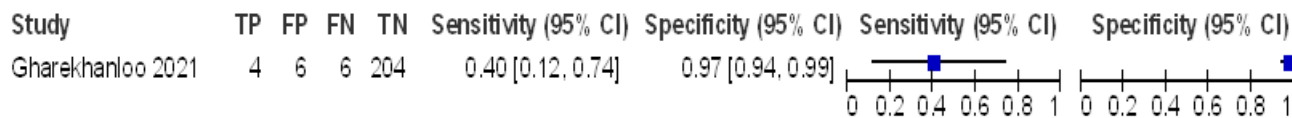
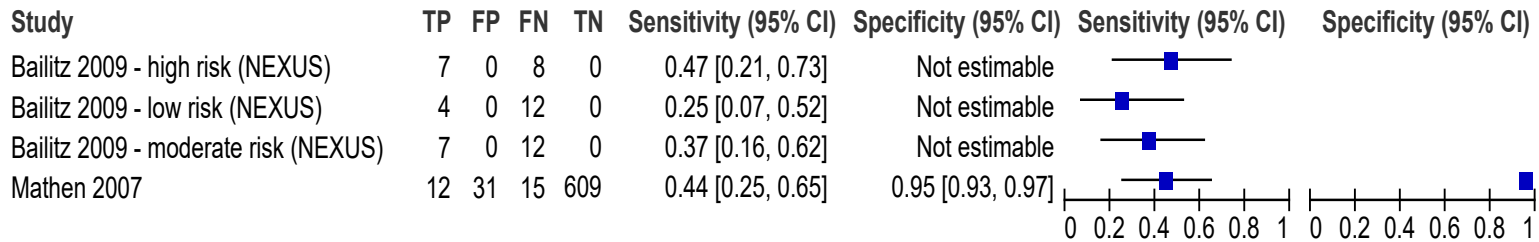
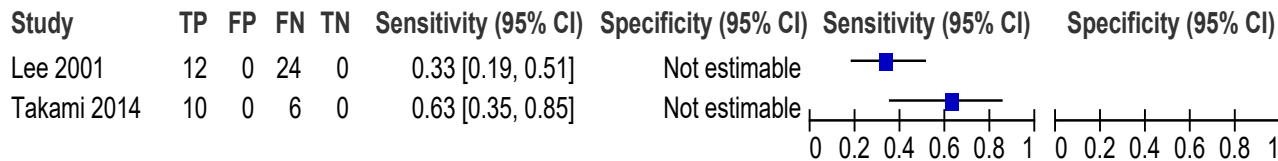


Figure 4: Those meeting at least one NEXUS criterion, unclear if head injury, final diagnosis as reference standard, clinically significant injury as outcome



Note that for the three Baillitz 2009 analyses, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for these analyses.

Figure 5: Any following trauma, unclear if head injury, CT as reference standard, cervical spine fractures as outcome



Note that for both studies, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for these analyses.

Figure 6: Any with blunt trauma, unclear if head injury, MRI as reference standard, ligamentous cervical spine injury as outcome

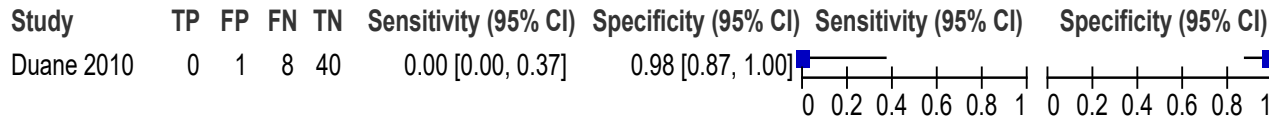
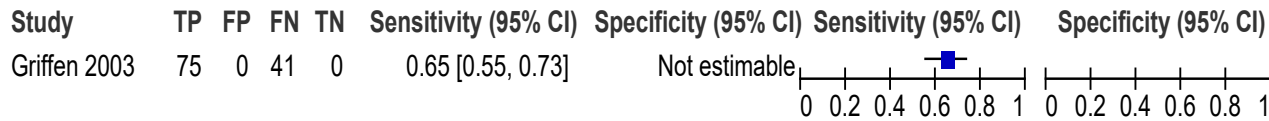
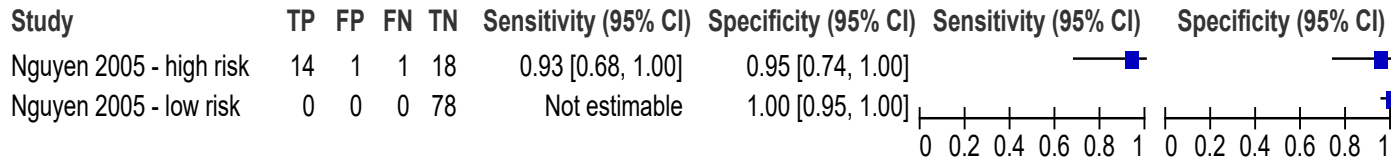


Figure 7: Any with blunt injury and cervical spine assessed, unclear if head injury, reference standard unclear/final diagnosis, cervical spine injuries as outcome



Note that for this study, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for this analysis.

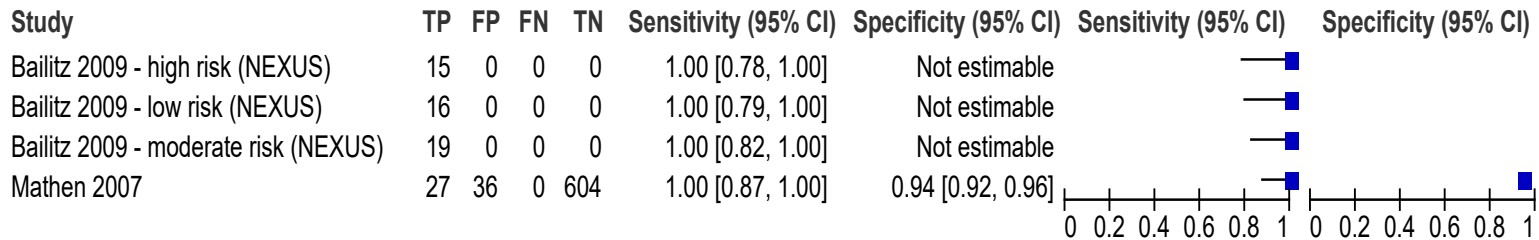
Figure 8: Any with blunt injury and cervical spine assessment, unclear if head injury, reference standard unclear/final diagnosis, cervical spine fractures as outcome



Note that for the low-risk analysis, sensitivity could not be calculated as there were no references standard positives in this group..

E.1.1.2 CT as index test

Figure 9: Those meeting at least one NEXUS criterion, unclear if head injury, final diagnosis as reference standard, clinically significant injury as outcome



Note that for the three Bailitz 2009 analyses, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for these analyses.

Figure 10: Those failing NEXUS low risk criteria, unclear if head injury, final diagnosis as reference standard, clinically significant fractures as outcome

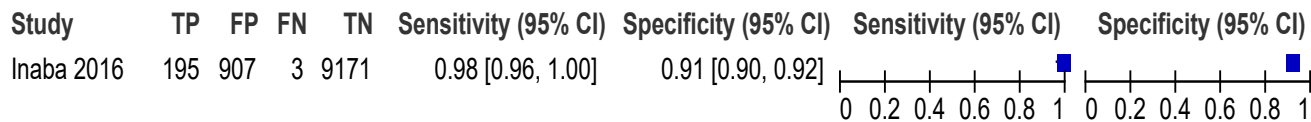
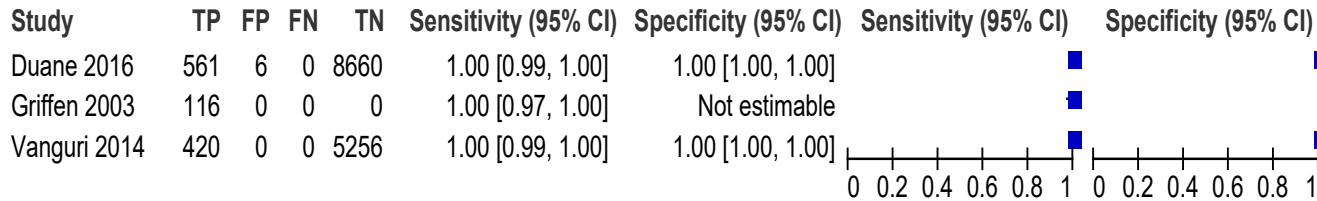
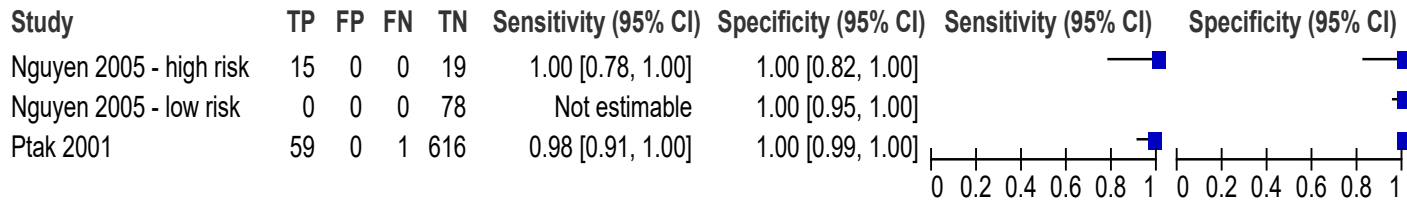


Figure 11: Any with blunt injury and cervical spine assessed, unclear if head injury, reference standard unclear/final diagnosis, cervical spine injuries as outcome



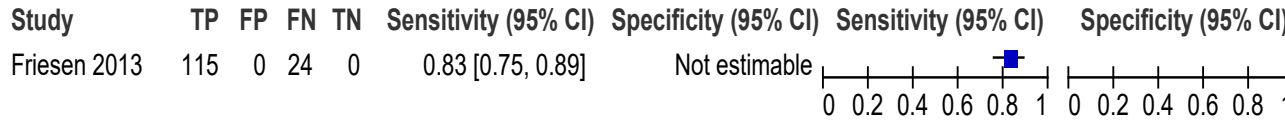
Note that for the Griffen 2003 study, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for this analysis.

Figure 12: Any with blunt injury and cervical spine assessment, unclear if head injury, reference standard unclear/final diagnosis, cervical spine fractures as outcome



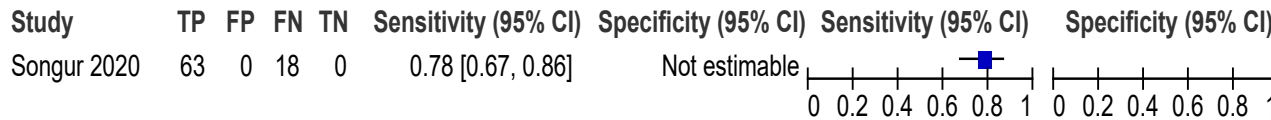
Note that for the Nguyen 2005 low-risk analysis, sensitivity could not be calculated as there were no references standard positives in this group..

Figure 13: Any with suspected blunt cervical spine injury, >75% with head CT, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome



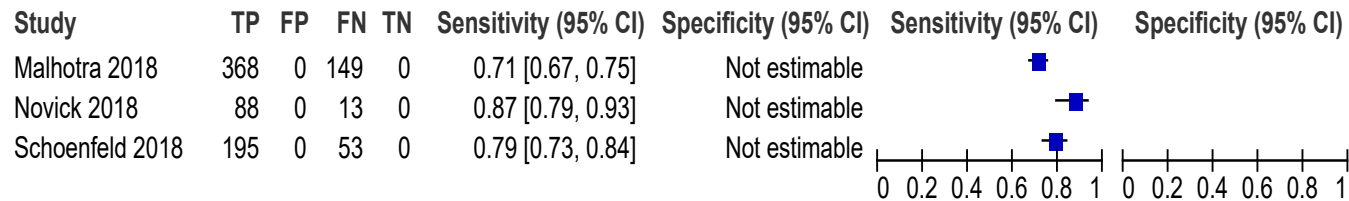
Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=67 were negative on both CT and MRI, representing true negatives but not input into plot as false specificity of 100% calculated)

Figure 14: Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome



Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=7 were negative on both CT and MRI, representing true negatives but not input into plot as false specificity of 100% calculated)

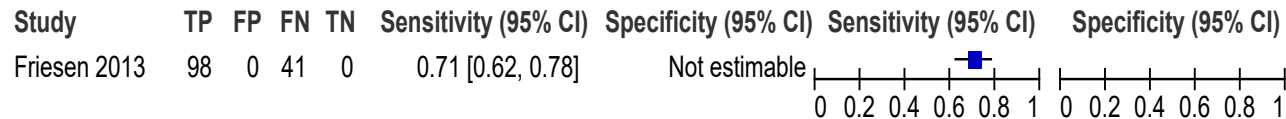
Figure 15: Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome



Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=563, n=140 and n=420 were negative on both CT and MRI in Malhotra 2018, Novick 2018 and Schoenfeld 2018, respectively,, representing true negatives but not input into plot as false specificity of 100% calculated)

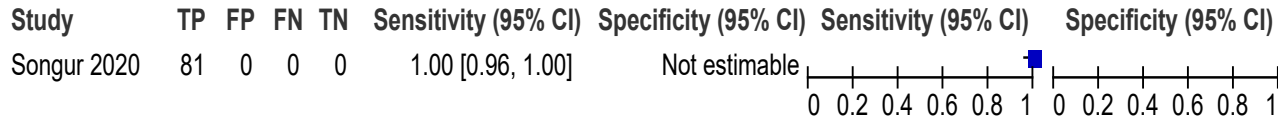
E.1.1.3 MRI as index test

Figure 16: Any with suspected blunt cervical spine injury, >75% with head CT, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome



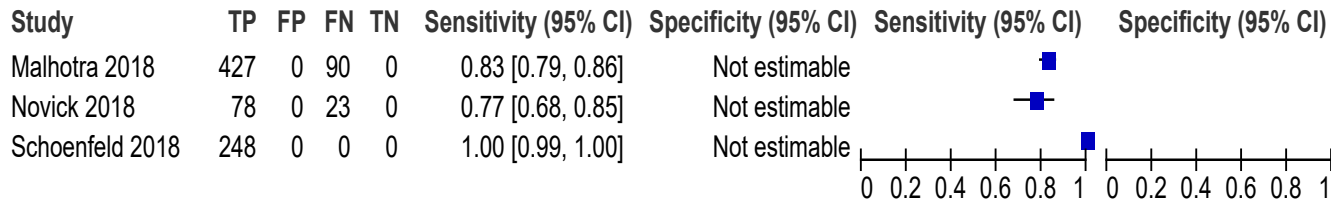
Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=67 were negative on both CT and MRI, representing true negatives but not input into plot as false specificity of 100% calculated)

Figure 17: Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome



Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=7 were negative on both CT and MRI, representing true negatives but not input into plot as false specificity of 100% calculated)

Figure 18: Any with suspected blunt cervical spine injury, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome

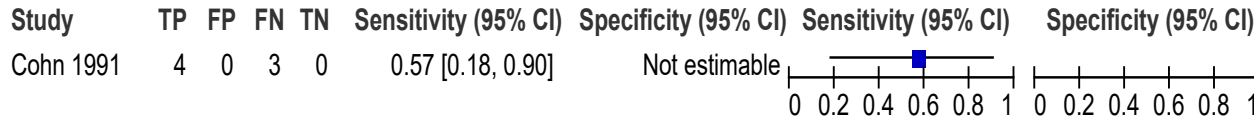


Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=563, n=140 and n=420 were negative on both CT and MRI in Malhotra 2018, Novick 2018 and Schoenfeld 2018, respectively,, representing true negatives but not input into plot as false specificity of 100% calculated)

those subsequently discharged following index test

E.1.2.1 X-ray as index test

Figure 19: Any admitted with blunt injury and cervical spine assessed, unclear if head injury, reference standard unclear/final diagnosis, cervical spine injuries as outcome



Note that for this study, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for this analysis.

Figure 20: Any admitted following trauma, unclear if head injury, CT as reference standard, cervical spine fractures as outcome

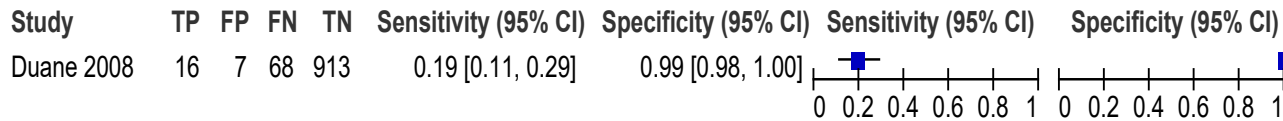
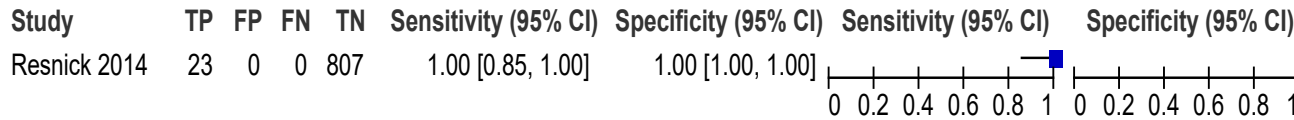


Figure 21: Any admitted following injury and cervical spine assessed, unclear if head injury, final diagnosis as reference standard, clinically significant cervical spine injuries as outcome



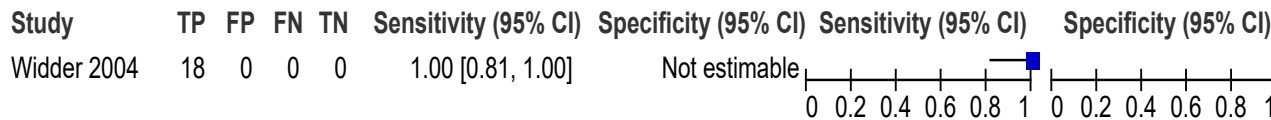
E.1.3 Adults – only including those that are obtunded, unconscious and/or requiring intensive care unit admission

E.1.3.1 CT as index test

Figure 22: High risk trauma patients (pain, neurological symptoms or obtundation), unclear if head injury, final diagnosis as reference standard, any cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Adams 2006).

Figure 23: High risk severely injured patients, unclear if head injury, final diagnosis as reference standard, cervical spine abnormality as outcome



Note that for this study, FP and TN were not reported and values were not necessarily zero. Only sensitivity could be calculated for this analysis.

Figure 24: High risk blunt trauma and admission to intensive care unit, unclear if head injury, final diagnosis as reference standard, unstable cervical spine injury as outcome

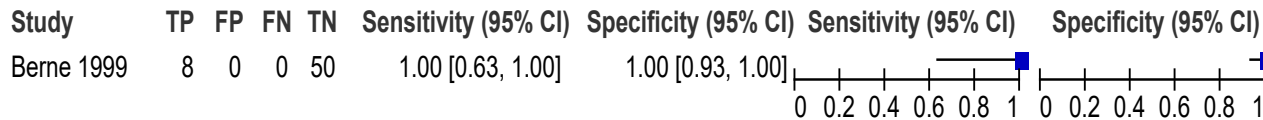


Figure 25: Unconscious intubated trauma patients, unclear if head injury, final diagnosis as reference standard, unstable cervical spine injury as outcome

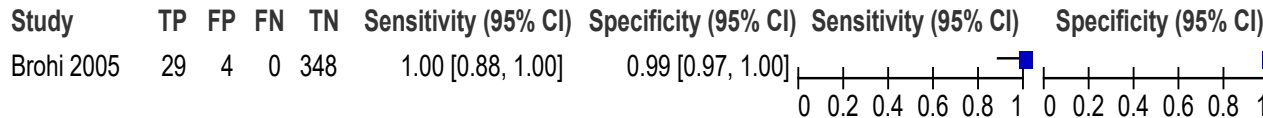


Figure 26: Altered sensorium admitted following injury and cervical spine assessed, unclear if head injury, final diagnosis as reference standard, clinically significant cervical spine injuries as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Raza 2013).

Figure 27: Obtunded with intracranial haemorrhage diagnosis following non high-impact trauma, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Tan 2014).

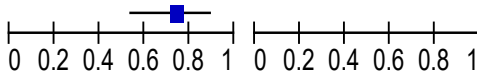
Figure 28: Obtunded patients, possibly all had brain assessment, CT + MRI as reference standard (only sensitivity possible), any cervical spine injuries as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Lau 2018).

Figure 29: Obtunded patients (mostly adults), unclear if head injury, CT + MRI as reference standard (only sensitivity possible), clinically significant cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Fisher 2013).

Figure 30: Unconscious adults, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Parmar 2018	20	0	7	0	0.74 [0.54, 0.89]	Not estimable		

Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=0 were negative on both CT and MRI, representing true negatives)

E.1.3.2 MRI as index test

Figure 31: Obtunded with intracranial haemorrhage diagnosis following non high-impact trauma, CT + MRI as reference standard (only sensitivity possible), unstable cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Tan 2014).

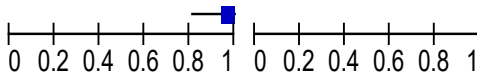
Figure 32: Obtunded patients, possibly all had brain assessment, CT + MRI as reference standard (only sensitivity possible), any cervical spine injuries as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Lau 2018).

Figure 33: Obtunded patients (mostly adults), unclear if head injury, CT + MRI as reference standard (only sensitivity possible), clinically significant cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Fisher 2013).

Figure 34: Unconscious adults, unclear if head injury, CT + MRI as reference standard (only sensitivity possible), any cervical spine injury as outcome

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Parmar 2018	26	0	1	0	0.96 [0.81, 1.00]	Not estimable		

Note that false positives are not possible when the index test forms part of reference standard, meaning specificity cannot be calculated (n=0 were negative on both CT and MRI, representing true negatives)

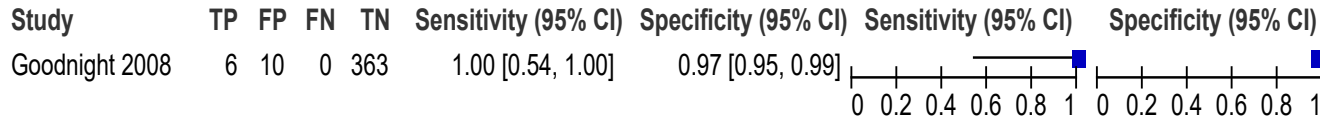
E.1.4 Adults – other very specific populations

E.1.4.1 X-ray as index test

Figure 35: Those with diffuse idiopathic skeletal hyperostosis with low energy trauma, unclear if head injury, whole spine CT as reference standard, acute fracture of cervical spine as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Dan Lantsman 2020).

Figure 36: Those with blunt trauma with CT and flexion-extension radiographs for continued cervical pain (fractures already excluded), unclear if head injury, all available evidence as reference standard, ligamentous cervical spine injury as outcome



E.1.4.2 CT as index test

Figure 37: Intoxicated adults with blunt trauma, unclear if head injury, final/discharge diagnosis as reference standard, unstable cervical spine injury as outcome

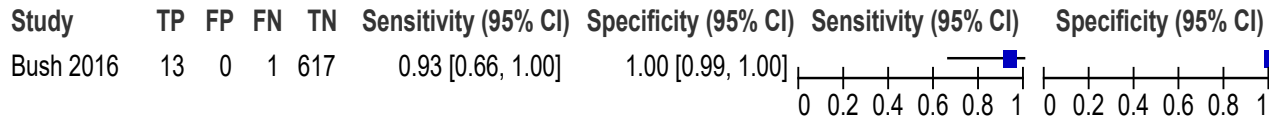
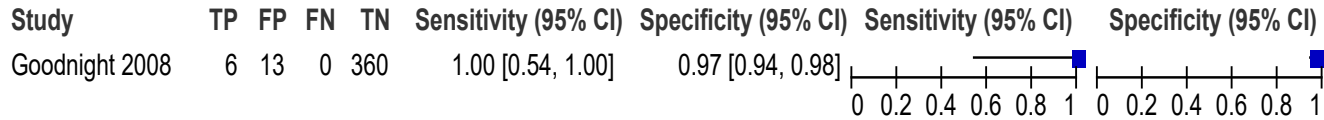


Figure 38: Those with blunt trauma with CT and flexion-extension radiographs for continued cervical pain, unclear if head injury, all available evidence as reference standard, ligamentous cervical spine injury as outcome



E.1.5 Children – all having index test and not limited to those that were admitted

E.1.5.1 X-ray as index test

Figure 39: Children with possible neck injury, 40% had head CT, reference standard unclear/follow-up/other imaging, cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Somppi 2018).

Figure 40: Children with cervical spine imaging, unclear if head injury, reference standard as CT, cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Rana 2009).

Figure 41: Children with possible neck injury, 40% had head CT, reference standard unclear/follow-up/other imaging, cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Somppi 2018).

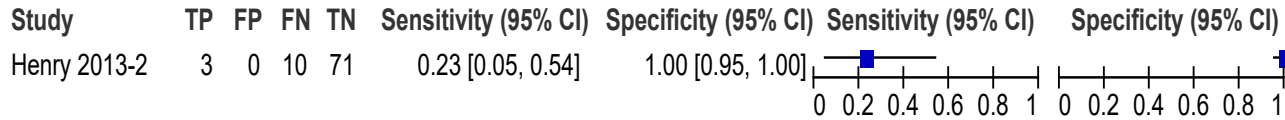
Figure 42: Children with cervical spine imaging, unclear if head injury, reference standard as other imaging findings (unclear), cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Rana 2009).

Figure 43: Children following trauma, unclear if head injury, reference standard as final diagnosis/unclear, unstable cervical spine injuries as outcome

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Derderian 2019	33	28	0	160	1.00 [0.89, 1.00]	0.85 [0.79, 0.90]		

Figure 44: Children following trauma, unclear if head injury, reference standard as MRI, any soft tissue cervical spine injury as outcome



E.1.5.3 MRI as index test

Figure 45: Children with possible neck injury, 40% had head CT, reference standard unclear/follow-up/other imaging, cervical spine injury as outcome

Raw data not reported and Forest Plot could therefore not be generated. Results are provided in GRADE tables as reported in the paper (Somppi 2018).

Figure 46: Children following trauma, unclear if head injury, reference standard as final diagnosis/unclear, unstable cervical spine injuries as outcome

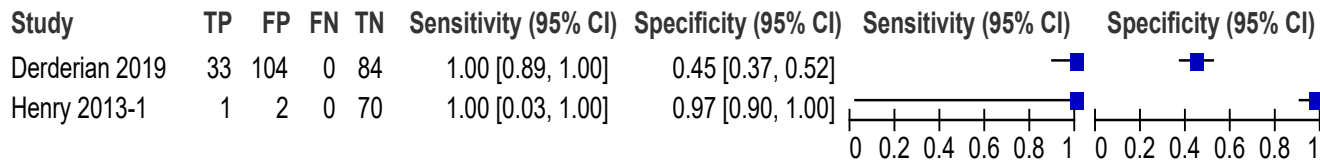
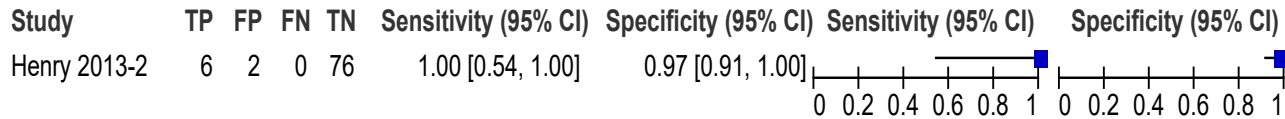


Figure 47: Children following trauma, unclear if head injury, reference standard as CT, any osseous cervical spine injury as outcome



E.1.6 Children – only including those that are obtunded, unconscious and/or requiring intensive care unit admission

E.1.6.1 X-ray as index test

Figure 48: Children with severe injuries admitted to intensive care unit, unclear if head injury, reference standard as clinical outcome/diagnosis at time of discharge/latest follow-up, cervical spine instability requiring surgery as outcome

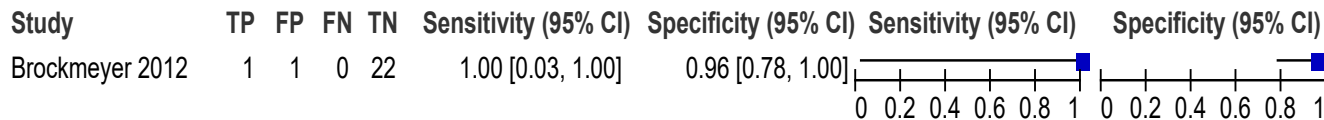


Figure 49: Children with cervical spine assessment and confirmed severe traumatic brain injury, reference standard as CT + MRI possibly other imaging, unstable cervical spine injury as outcome

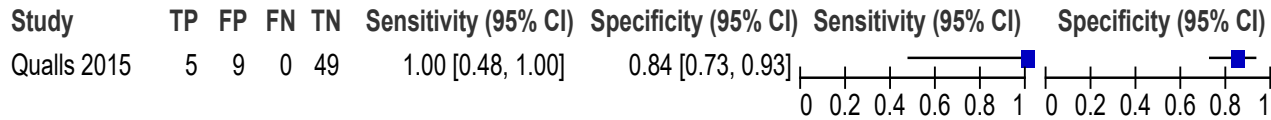


Figure 50: Children with severe injuries/unconscious, unclear if head injury, reference standard as final diagnosis/all information, injuries requiring stabilisation/surgical correction as outcome

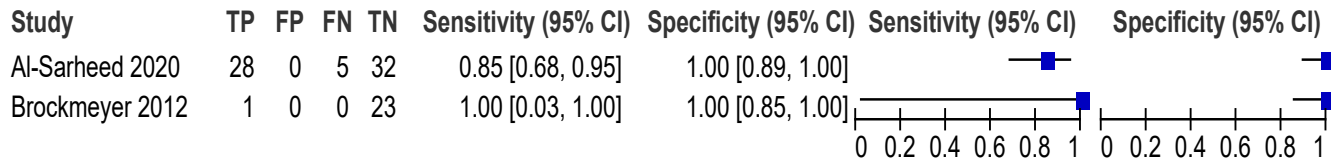


Figure 51: Children with cervical spine assessment and confirmed severe traumatic brain injury, reference standard as CT + MRI possibly other imaging, unstable cervical spine injury as outcome

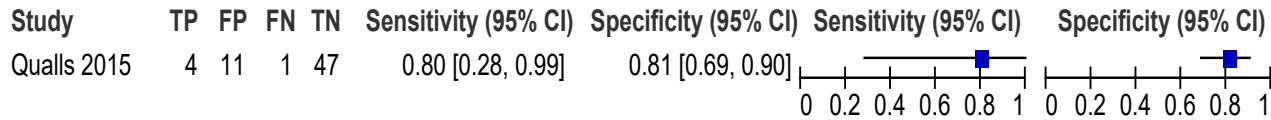
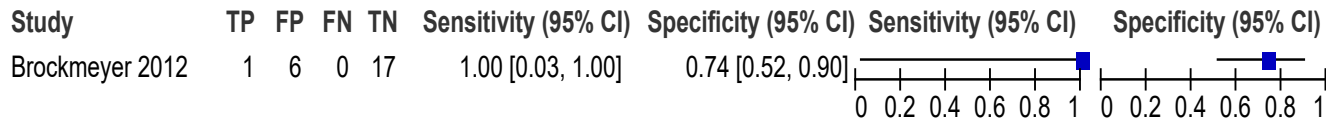
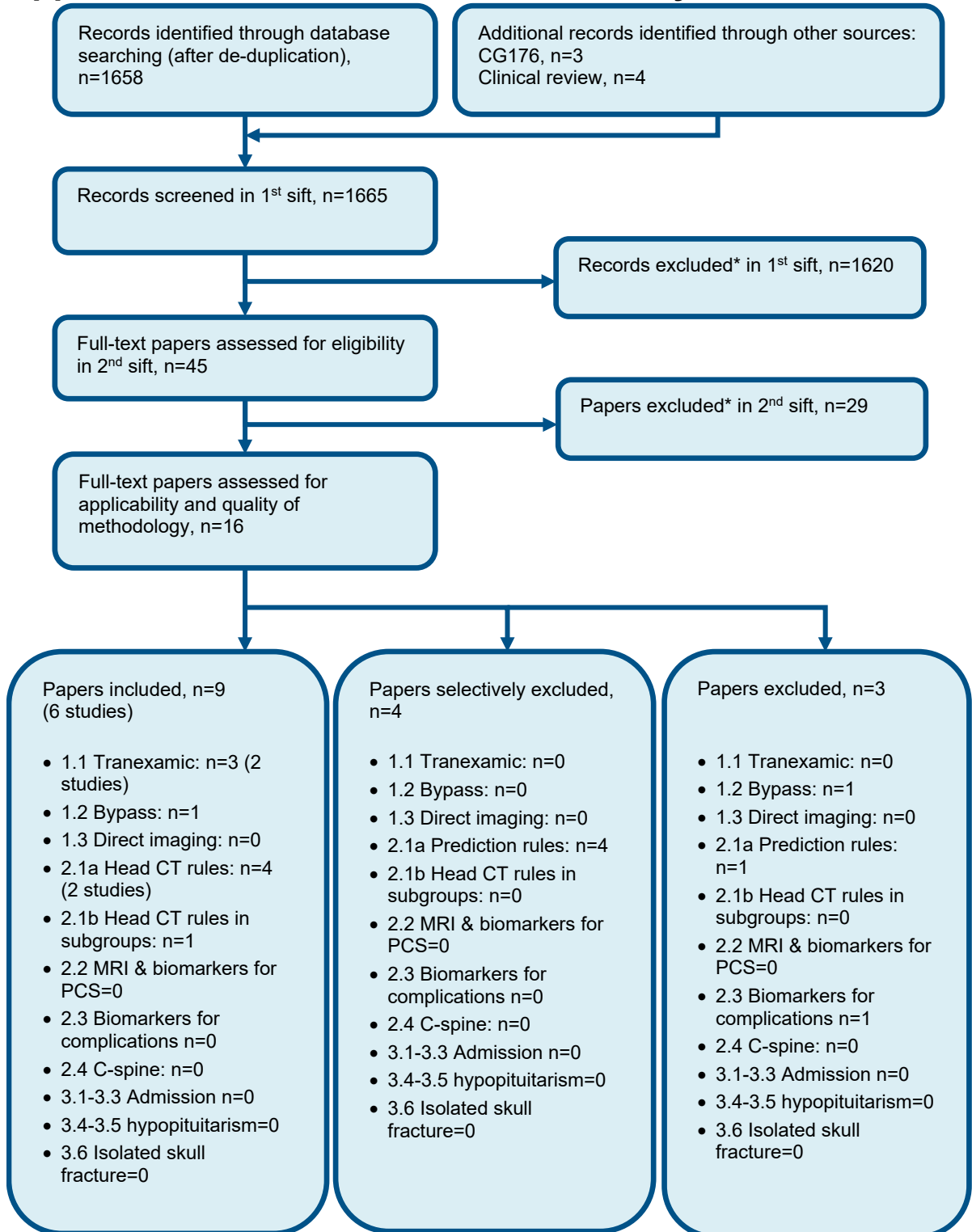


Figure 52: Children with severe injuries admitted to intensive care unit, unclear if head injury, reference standard as clinical outcome/diagnosis at time of discharge/latest follow-up, cervical spine instability requiring surgery as outcome



Appendix F – Economic evidence study selection



* Non-relevant population, intervention, comparison, design or setting; non-English language

- 1 **Appendix G – Economic evidence tables**
- 2 None.

Appendix H – CG176 Health economic model (2014)

H.1 Methods

H.1.1 Model overview

Head injury (HI) patients can sustain bony and/or soft tissue injuries to the cervical (C) spine. Whether patients experience a soft tissue injury becomes relevant after the initial imaging shows a bony injury, or if the initial imaging is negative but the clinical picture still suggests that there is a high risk of a cervical spine injury (CSI), in which case patients will experience solely a soft tissue injury of the C-spine.

CG56 included a tentative cost analysis on this topic, with the comparison between the NEXUS and the Canadian CT rule for CSI prediction. It was estimated that the Canadian rule could save from £4 to £14 per patient to the NHS. However, this cost analysis had limited validity due to the use of overseas data and simplified assumptions with regards to dealing with indeterminate diagnostic imaging results.

The management of patients with HI and suspected CSI is particularly challenging in terms of resource implications. The main trade offs for this topic are represented by the cost of the diagnostic tests (whether X-ray, CT scan and MRI) versus the failure to detect their CSI (false negatives).

The guidelines update of the CG56 literature review found no new economic evidence since the publication of CG56 on the cost-effectiveness of clinical prediction rules for any of the clinical questions for this topic.

As a consequence, the GC has identified this topic as a high priority for an original economic analysis.

The economic analysis will address the following clinical question:

Q1. What is the best clinical prediction rule for determining which patients with head injury should be imaged (initial imaging with X-ray or CT) for cervical spine injury?

H.1.1.1 Comparators

Seven clearance strategies for patients with HI and suspected CSI were devised to allow for differential use of diagnostic imaging.

The strategies compared in this cost-effectiveness analysis are:

- **CT on all:** In this strategy, no prediction rule is used. Everyone with HI and suspected CSI is given a CT scan.
- **X-ray on all:** In this strategy, no prediction rule is used. Everyone with HI and suspected CSI is given an X-ray.
- **CT according to NEXUS:** In this strategy, the NEXUS prediction rule is used to determine whether a CT scan is necessary. Only under the direction of the NEXUS prediction rule is a CT scan undertaken.
- **CT according to Canadian C-Spine:** In this strategy, the Canadian C-spine prediction rule is used to determine whether a CT scan is necessary. Only under the direction of the Canadian C-spine prediction rule is a CT scan undertaken.
- **X-ray according to NEXUS:** In this strategy, the NEXUS prediction rule is used to determine whether an X-ray is necessary. Only under the direction of the NEXUS prediction rule is an X-ray undertaken.

- **X-ray according to Canadian C-spine:** In this strategy, the Canadian C-spine prediction rule is used to determine whether an X-ray is necessary. Only under the direction of the Canadian C-spine prediction rule is an X-ray undertaken.
- **No imaging:** In this strategy, patients with HI and suspected CSI do not receive any diagnostic imaging.

The CT on all, X-ray on all, and No imaging strategies were included as theoretical strategies to explore the overall cost-effectiveness of diagnostic imaging. In practice, the first two strategies are not feasible and the last is not acceptable.

H.1.1.2 Population

The population of the model consists of patients over the age of 16 with HI and suspected CSI.

H.1.1.3 Time horizon, perspective, discount rates used

The analysis took the perspective of the UK NHS. The time horizon of the model was one in-hospital episode including diagnosis and treatment, discounting was therefore not applicable.

H.1.1.4 Deviations from NICE reference case

The search for quality of life evidence did not identify any data which the GC felt applicable to inform the expected health benefits for each diagnostic outcome. With long-term management of CSI patients falling outside of the scope of this guideline, accurate data on the long-term health outcomes and resource use associated with downstream management were not available.

As a compromise, the GC identified the cost of prevention of a false negative as the most useful outcome for decision making and cautioned the interpretation of results due to the lack of evaluation of all of the trade offs involved between the diagnostic outcomes (such as the benefit of true positives and negatives, and the health cost of the false positive, noting cost of treating a false negative case was included in the analysis). To further assess the net cost of avoiding a false negative, a range of potential litigation costs of a false negative was incorporated in a threshold sensitivity analysis. Also, a conservative hypothetical scenario where minimal QALY gain was associated with a true positive and zero health or monetary cost associated with the false diagnostic outcomes was analysed.

There is divergence from the NICE reference case as the main analysis is a cost-effectiveness analysis (rather than a CUA) assessing the cost per diagnostic outcome in a time horizon limited to the diagnostic workup and short-term management. In addition, we employ the litigation cost which may be associated to a false negative and the underlying assumption that no clinical harm or cost (other than that of initial treatment) is associated to patients who have a false positive test result to assess cost-effectiveness. This further analysis is in essence a cost minimisation analysis.

H.1.1.5 Uncertainty

The base case analysis employs expected values of costs, utilities and probabilities for model parameters and serves as base case analysis. If there are uncertainties about the values and assumptions used in the main cost-effectiveness analysis, sensitivity analyses are conducted. Results from base case and sensitivity analyses are compared.

There are two types of sensitivity analysis.

Deterministic Sensitivity Analysis (DSA) is where the value of one of the parameters is changed to observe any effect on the results. This allows determination of the threshold at which a parameter's value is likely to change the conclusion. The GC were uncertain about a number of parameters: the prevalence of CSI in a population, the cost of no procedure for patients with and without CSI, the clinical decision for further imaging after an initial X-ray / CT, and the specifications of initial imaging strategies (the probability of being given CT/X-ray/no imaging initially) and these uncertainties were tested by deterministic sensitivity analysis.

Probabilistic Sensitivity Analysis (PSA) is conducted to quantify parameter uncertainty. For every parameter subject to uncertainty (i.e. unit costs, sensitivities and specificities of the prediction rules and clinician estimates), a distribution is assigned to reflect its uncertainty. Random draws across all parameter distributions are undertaken using Monte Carlo methods. This process is repeated many times to build up a simulated sample of the expected value of the model output parameters, as well as a quantification of parameter uncertainty. The PSA will determine the probability an intervention is cost-effective given a particular cost-effectiveness threshold.

H.1.2 Approach to modelling

The model is a decision tree which includes evidence on the prevalence of CSI among patients with head injury as well as on intermediate outcomes (specificity and sensitivity) of all strategies being compared (for example X-rays, CT scans, MRI, prediction rules). The combination of the prevalence of CSI with the specificity and sensitivity of each strategy determines the proportion of patients who have abnormal, indeterminate and normal imaging results. According to diagnostic imaging results, patients undergo a specific type of medical management (observation, immediate discharge or surgical and non-surgical treatment). The model tracks the number of patients for whom the clinical decision is appropriate (TP, TN) or inappropriate (FP, FN).

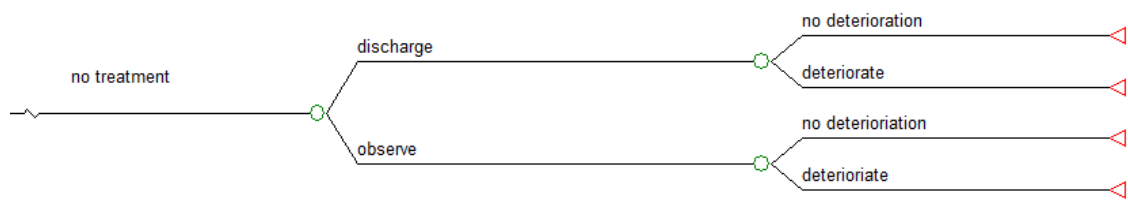
As there was limited data availability for survival and medical events (such as long term disability) following medical interventions received or not received by patients, the most important health outcome was considered to be the number of false negatives identified by each strategy.

H.1.2.1 Model structure

There are 7 clearance strategies for all patients with HI and suspected CSI regardless of the presence or absence of CSI. These seven strategies are described in M.1.1.1.

For Strategies 1 - 7 where no initial imaging is undertaken, patients are treated as normal, receive no treatment and are either discharged or observed in hospital for a period of 1 week (see Figure 67). If patients have CSI, they may or may not experience deterioration. If patients do not have CSI, they do not experience deterioration.

Figure 53 Model structure for No Initial Imaging



For strategies 2-7 when initial imaging is a CT scan, further imaging may take place according to the initial CT scan result.

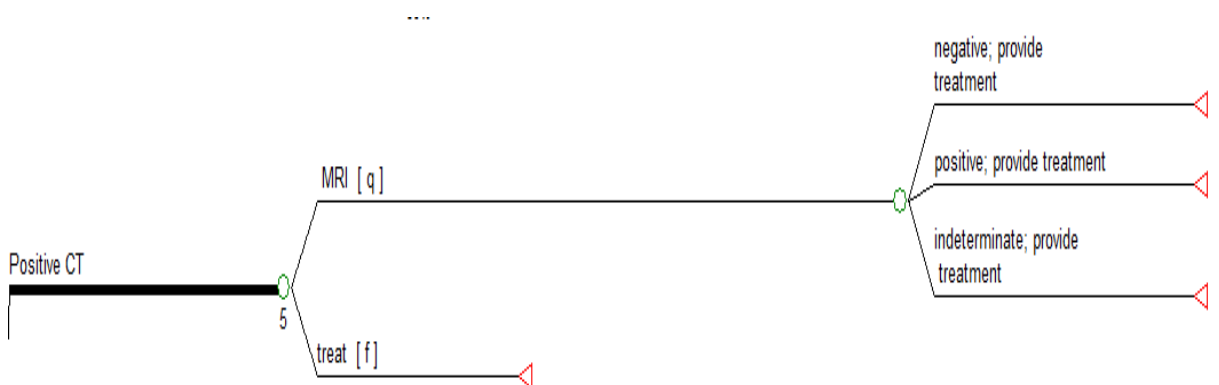
If the initial CT result is negative (normal), patients are given no further tests and discharged (see Figure 68).

Figure 54 Model structure for initial CT scan and negative (normal) result



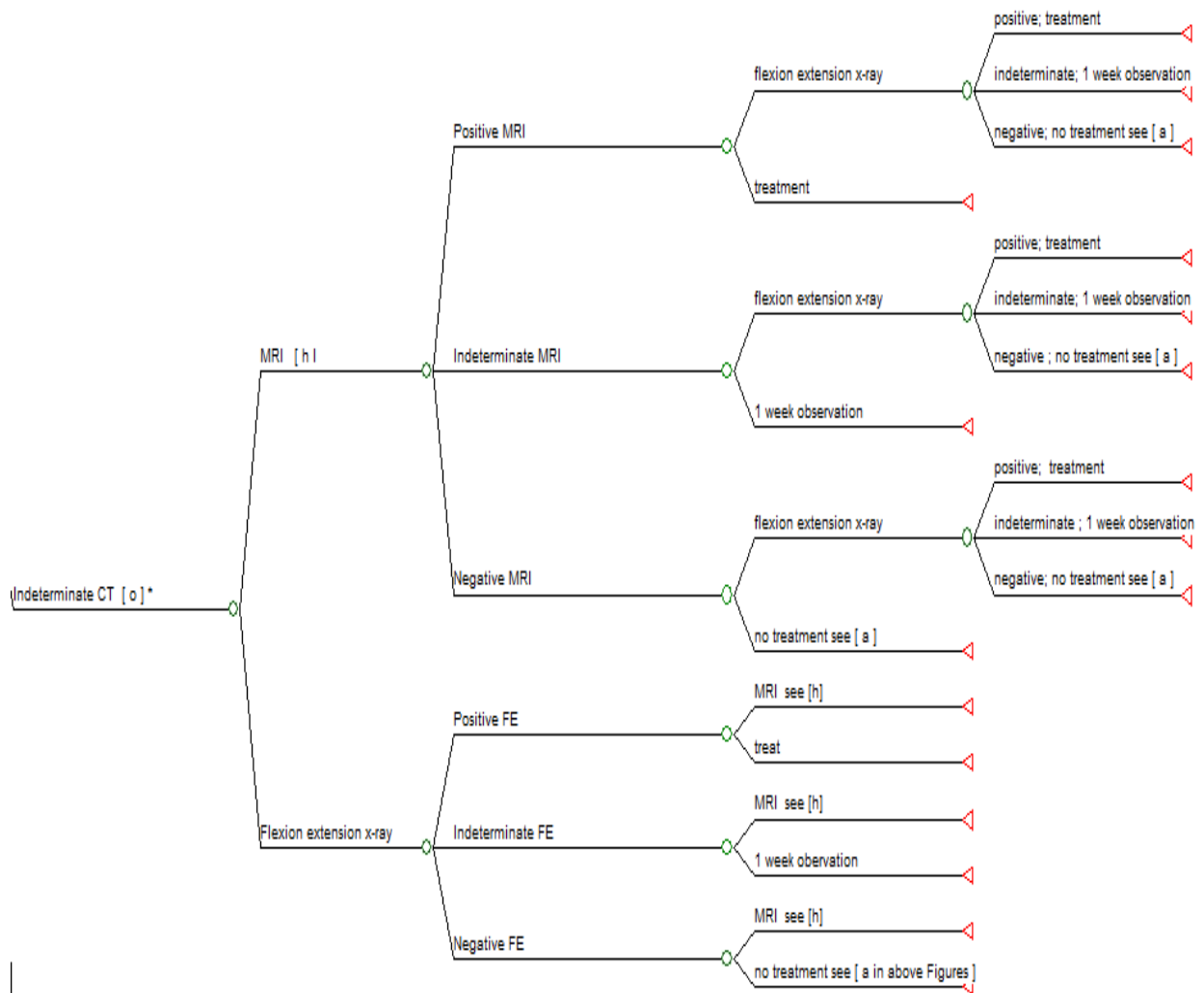
If the initial CT scan result is positive (abnormal), the patient may be treated immediately or provided a further MRI before treatment (see Figure 69).

Figure 55 Model structure for initial CT scan and positive (abnormal) result



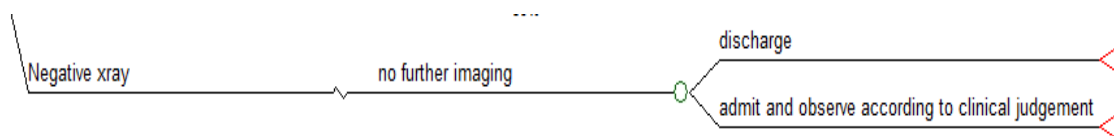
If the initial CT scan is indeterminate (Figure 70), the patient will undergo further diagnostic imaging -- MRI or Flexion Extension (FE). If the second diagnostic imaging (MRI/FE) is positive, the patient may be treated immediately or given a third diagnostic scan (MRI/FE). Patients are treated if the third diagnostic scan is positive. Patients are observed in hospital for a one week period if the third diagnostic scan is indeterminate. Patients receive no further diagnostic imaging and are discharged if the third diagnostic scan is negative.

Figure 56 Model structure for initial CT scan and indeterminate result



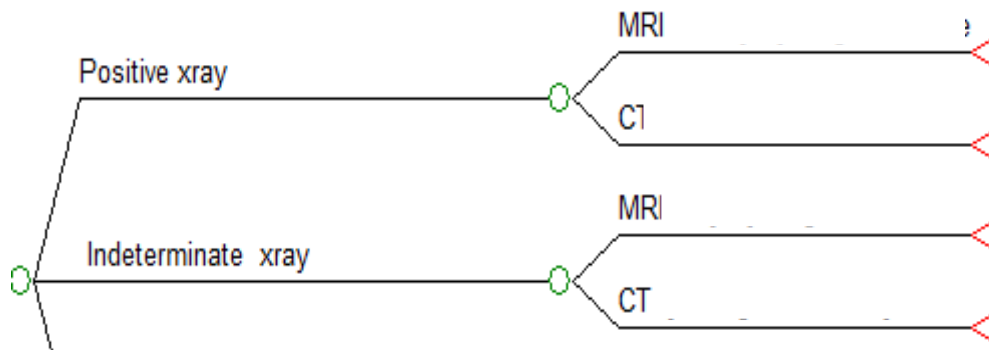
When initial imaging is an X-ray, further imaging can occur according to its results. A negative initial x rya result warrants no further imaging and patients are either discharged or admitted one week observation in hospital according to clinical judgement (Figure 71).

Figure 57 Model structure for initial X-ray and negative result



A positive or indeterminate X-ray result requires further imaging (MRI / CT). The model structure following a MRI/CT scan is summarised in Figure 72. As the model structure here is the same as those described and illustrated above, refer to Figure 68, Figure 69, and Figure 70, for details of the model structure following a CT scan and Figure 70, branch [h] for details of the model structure following an MRI).

Figure 58 Model structure for initial X-ray and positive / indeterminate result



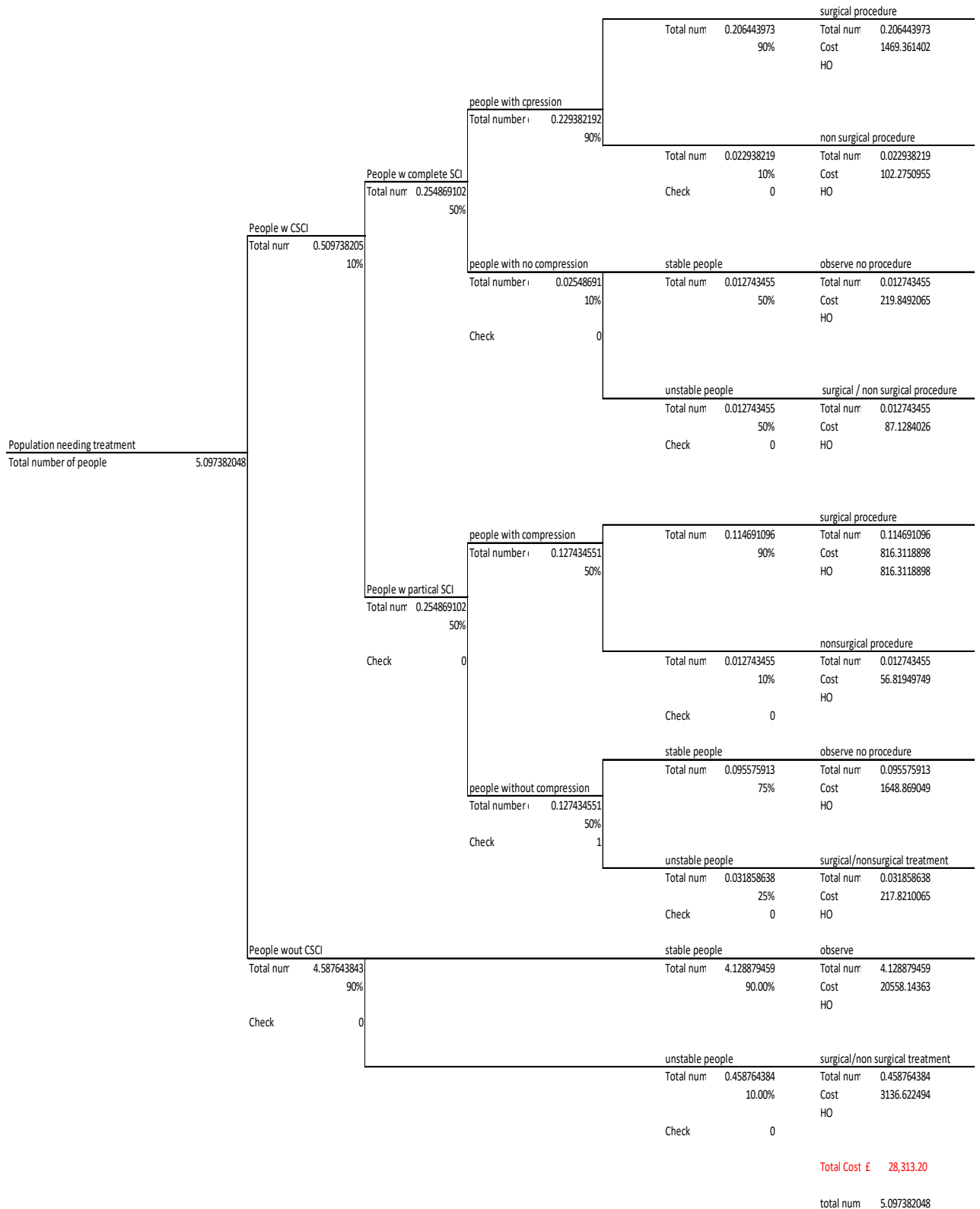
Patients who need treatment are provided specific procedures according to injury characteristics. Specifically, the GDG judged that the characteristics of a Cervical Spine Injury – bone; ligamentous; compression; stability; and presence of (Cervical Spinal Cord Injury) SCI— would determine the type of treatment required. The tree structure detailed in Figure 73 show the subcategorisation of injury characteristics and the appropriate corresponding procedure.

Patients with complete or partial SCI and compression required a surgical or non-surgical procedure. Those who require surgery receive decompression and, where necessary, fusion. A collar could be provided in the case that a non-surgical procedure is deemed appropriate.

Patients with partial or complete SCI and no compression were treated according to the stability of their injury. When the injury is stable, no procedure was necessary and instead, patients would receive a period of hospital observation. If the injury was unstable, a surgical or non-surgical procedure is required.

Some patients with cervical spine injury will not have SCI. When these patients have stable injuries, then no procedure is required. Instead, they receive a period of hospital observation. However, if these patients sustain an unstable injury, surgical or non-surgical treatment is needed.

Figure 59 Model structure for patients who require treatment



H.1.3 Model inputs

H.1.3.1 Summary table of model inputs

Model parameters were based on clinical evidence identified in the systematic review undertaken for the guideline and supplemented by additional data sources when necessary. For example, a recent economic paper, Harlpen et al.²⁴, was considered to be the best available source in the absence of a full systematic review on the diagnostic accuracy of the imaging modalities contained within the model. The authors had conducted a systematic search on these parameters, and several sources were used to inform the estimates used.

Model inputs were validated with clinical members of the GDG. In all but one instance only one source was identified in the clinical review to inform accuracy estimates of the clinical decision rules. In the case of the rule to x-ray by Canadian C-spine there was more than one source identified. In clinical validation of the sources in regards to their applicability and quality, the developers considered Coffey et al.⁸ to be the only appropriate source to inform the model for the following reasons. Throughout the guideline the developers placed more emphasis on recent UK studies, with Coffey et al. being the only source for this parameter to be both derived and validated in the UK context.

A summary of the model inputs used in the base case (primary) analysis are provided in below. More details about sources, calculations and rationale for selection can be found in the sections following this summary table.

Table 30: Summary of base-case and sensitivity analysis model inputs

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Cohort Settings				
Patients with HI and no CSI/with HI and CSI	99.5%/0.5%	-	-	GC Expert Opinion
Cost of Prediction Rules (£)				
Canadian C-spine	£0	-	-	Criteria are freely accessible
NEXUS	£0	-	-	
Cost of Diagnostic Imaging (£)				
X-ray	£30	Best fit distribution identified according to methods described in section M.1.4, Table 70 .		Calculated from 2011-2012 NHS reference cost codes DAPF
Flexion, extension X-ray	£60			Calculated from 2011-2012 NHS reference cost codes DAPF and according to GDG Expert Opinion
CT	£104			Calculated from 2011-2012 NHS reference cost codes RA08A, RA11Z and RA13Z
MRI	£182			Calculated from 2011-2012 NHS reference cost codes RA01A & RA04Z
No imaging	£0			N/A
Cost of Treatment (£)				

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Surgical procedure	£7,117	Best fit distribution identified according to methods described in section M.1.4, Table 70 .		Calculated from 2011-2012 NHS reference cost code HC01-HC04
Surgical or Non-Surgical Procedure	£6,837			Calculated from 2011-2012 NHS reference cost code HC01-HC06
Non –Surgical Procedure	£ 4,459			Calculated from 2011-2012 NHS reference cost codes HC05-HC06
No procedure, (patients with SCI)	£17,252			Calculated from 2011-2012 NHS reference cost codes HC21B
No Procedure, (patients with no SCI)	£4,979			Calculated from 2011-2012 NHS reference cost code HC21C
Deterioration after treatment	£7,214			GC Expert Opinion
Discharge	£0			
Performance of Prediction Tools				
Canadian C-spine X-ray - Sensitivity	1.00	Beta	$\alpha = 8, \beta = 0$	Clinical Review- Coffey 2011 ⁸
Canadian C-spine X-ray - Specificity	0.43	Beta	$\alpha = 605, \beta = 807$	
Canadian C-spine CT - Sensitivity	1.00	Beta	$\alpha = 192, \beta = 0$	Clinical Review- Duane 2011A ¹⁵
Canadian C-spine CT - Specificity	0.06	Beta	$\alpha = 18, \beta = 2991$	
NEXUS X-ray - Sensitivity	0.91	Beta	$\alpha = 147, \beta = 15$	Clinical Review- Stiell 2003 ⁴⁵
NEXUS X-ray - Specificity	0.37	Beta	$\alpha = 2677, \beta = 4599$	
NEXUS CT - Sensitivity	0.90	Beta	$\alpha = 37, \beta = 4$	Clinical Review- Griffith 2011 ²³
NEXUS CT - Specificity	0.24	Beta	$\alpha = 364, \beta = 1160$	
Performance of X-ray				
Sensitivity	0.568	Beta	$\alpha = 334, \beta = 254$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	80%	Beta	$\alpha = 800, \beta = 200$	GC Expert Opinion
Abnormal results which are indeterminate	10%	Beta	$\alpha = 100, \beta = 900$	
Specificity	0.997	Beta	$\alpha = 45822, \beta = 138$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	10%	Beta	$\alpha = 100, \beta = 900$	GC Expert Opinion
Abnormal results which are indeterminate	80%	Beta	$\alpha = 800, \beta = 200$	

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Performance of CT				
Sensitivity	0.832	Beta	$\alpha = 1545, \beta = 312$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	90%	Beta	$\alpha = 900, \beta = 100$	GC Expert Opinion
Abnormal results which are indeterminate	10%	Beta	$\alpha = 100, \beta = 900$	
Specificity	0.999	Beta	$\alpha = 15335, \beta = 15$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	10%	Beta	$\alpha = 100, \beta = 900$	GC Expert Opinion
Abnormal results which are indeterminate	90%	Beta	$\alpha = 900, \beta = 100$	
Performance of MRI				
Sensitivity	0.867	Beta	$\alpha = 386, \beta = 59$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	10%	Beta	$\alpha = 100, \beta = 900$	GC Expert Opinion
Abnormal results which are indeterminate	0%			
Specificity	0.997	Beta	$\alpha = 565, \beta = 2$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	10%	Beta	$\alpha = 100, \beta = 900$	GC Expert Opinion
Abnormal results which are indeterminate	0%			
Performance of FE-X-ray				
Sensitivity	0.568	Beta	$\alpha = 334, \beta = 254$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	70%	Beta	$\alpha = 700, \beta = 300$	GC Expert Opinion
Abnormal results which are indeterminate	20%	Beta	$\alpha = 200, \beta = 800$	
Specificity	0.997	Beta	$\alpha = 45822, \beta = 138$	Clinical Review- Halpern 2010 ²⁴
Normal results which are indeterminate	90%	Beta	$\alpha = 900, \beta = 100$	GC Expert Opinion
Abnormal results which are indeterminate	50%	Beta	$\alpha = 500, \beta = 500$	
Clinical events (Positive Cases—Patients with CSI)				

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
After no imaging				GC Expert Opinion
Probability clinician chooses immediate discharge	5%	Uniform	Min =4.5% , Max =5.5%	
Probability clinician chooses observation then discharge	95%	Uniform	Min = 85.5%, Max =100%	
After no imaging & discharge				
Probability deteriorate	95.0%	Uniform	Min = 85.5%, Max =100%	
Probability no deterioration	5.0%	Uniform	Min = 4.5%, Max =5.5%	
After no imaging & observe				
Probability deteriorate	20.0%	Uniform	Min = 18%, Max =22%	
Probability no deterioration	80.0%	Uniform	Min = 72%, Max =88%	
After abnormal initial CT result				
Probability clinician chooses MRI again	70%	Uniform	Min = 63%, Max =77%	
Probability clinician chooses to treat	30%	Uniform	Min = 27%, Max =33%	
After indeterminate initial CT result				
Probability clinician chooses MRI again	60%	Uniform	Min = 54%, Max =66%	
Probability clinician chooses flexion/extension x-ray	40%	Uniform	Min = 36%, Max =44%	
After indeterminate CT and abnormal MRI				

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Probability clinician chooses flexion/extension x-ray	10%	Uniform	Min = 9%, Max = 11%	
Probability clinician chooses to treat	90%	Uniform	Min = 81%, Max = 99%	
After indeterminate CT and indeterminate MRI				
Probability clinician chooses flexion/extension x-ray	50%	Uniform	Min = 45%, Max = 55%	
Probability clinician chooses to observe	50%	Uniform	Min = 45%, Max = 55%	
After indeterminate CT and normal MRI				
Probability clinician chooses flexion/extension x-ray	20%	Uniform	Min = 18%, Max = 22%	
Probability clinician chooses to discharge	70%	Uniform	Min = 63%, Max = 77%	
Probability clinician chooses to observe 1 week	10%	Uniform	Min = 9%, Max = 11%	
After indeterminate CT and abnormal flexion-extension				
Probability clinician chooses to treat	5%	Uniform	Min = 4.5%, Max = 5.5%	
Probability clinician chooses MRI	95%	Uniform	Min = 85.5%, Max = 100%	
After indeterminate CT and indeterminately flexion-extension				

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source	
Probability clinician chooses to observe and discharge	1%	Uniform	Min = 0.9%, Max =1.1%		
Probability clinician chooses MRI	99%	Uniform	Min =89.1%, Max =100%		
After indeterminate CT and normal flexion-extension					
Probability clinician chooses to discharge	40%	Uniform	Min =36% , Max =44%		
Probability clinician chooses MRI	60%	Uniform	Min = 54%, Max =66%		
After first x-ray is abnormal					
Probability clinician chooses CT	95%	Uniform	Min =85.5%, Max =100%		
Probability clinician chooses MRI	5%	Uniform	Min = 4.5%, Max =5.5%		
After first x-ray is indeterminate					
Probability clinician chooses CT	99%	Uniform	Min =89.1%, Max =100%		
Probability clinician chooses MRI	1%	Uniform	Min = 0.9%, Max =1.1%		
After first x-ray is normal					
Probability clinician chooses discharge	95%	Uniform	Min =85.5%, Max =100%		
Probability clinician chooses observe	5%	Uniform	Min = 4.5%, Max =5.5%		
Clinical events (Negative Cases—Patients without CSI)					
After no imaging					GDG Expert Opinion
Probability clinician chooses immediate discharge	95%	Uniform	Min =85.5%, Max =100%		

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Probability clinician chooses observation then discharge	5%	Uniform	Min = 4.5%, Max =5.5%	
After abnormal initial CT result				
Probability clinician chooses MRI again	99%	Uniform	Min =89.1%, Max =100%	
Probability clinician chooses to treat	1%	Uniform	Min = 0.9%, Max =1.1%	
After indeterminate initial CT result				
Probability clinician chooses MRI again	90%	Uniform	Min =89.1%, Max =100%	
Probability clinician chooses flexion/extension x-ray	10%	Uniform	Min =9% , Max =11%	
After indeterminate CT and abnormal MRI				
Probability clinician chooses flexion/extension x-ray	10%	Uniform	Min = 9%, Max =11%	
Probability clinician chooses to treat	90%	Uniform	Min = 81%, Max =99%	
After indeterminate CT and indeterminate MRI				
Probability clinician chooses flexion/extension x-ray	35%	Uniform	Min =31.5%, Max =38.5%	
Probability clinician chooses to observe	65%	Uniform	Min =58.5%, Max =71.5%	

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
After indeterminate CT and normal MRI				
Probability clinician chooses flexion/extension x-ray	1%	Uniform	Min = 0.9%, Max = 1.1%	
Probability clinician chooses to discharge	98%	Uniform	Min = 88.2%, Max = 100%	
Probability clinician chooses to observe 1 wee ⁵²⁰ k	1%	Uniform	Min = 0.9%, Max = 1.1%	
After indeterminate CT and abnormal flexion-extension				
Probability clinician chooses to treat	10%	Uniform	Min = 9%, Max = 11%	
Probability clinician chooses MRI	90%	Uniform	Min = 81%, Max = 99%	
After indeterminate CT and indeterminate flexion-extension				
Probability clinician chooses to observe and discharge	5%	Uniform	Min = 4.5%, Max = 5.5%	
Probability clinician chooses MRI	95%	Uniform	Min = 85.5%, Max = 100%	
After indeterminate CT and normal flexion-extension				
Probability clinician chooses to discharge	50%	Uniform	Min = 45%, Max = 55%	

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source	
Probability clinician chooses MRI	50%	Uniform	Min = 45%, Max =55%		
After first x-ray is abnormal					
Probability clinician chooses CT	95%	Uniform	Min = 85%, Max =100%		
Probability clinician chooses MRI	5%	Uniform	Min = 4.5%, Max =5.5%		
After first x-ray is indeterminate					
Probability clinician chooses CT	99%	Uniform	Min =89.1% Max =100%		
Probability clinician chooses MRI	1%	Uniform	Min = 0.9%, Max =1.1%		
After first x-ray is normal					
Probability clinician chooses discharge	95%	Uniform	Min = 85%, Max =100%		
Probability clinician chooses observe	5%	Uniform	Min = 4.5%, Max =5.5%		
Clinical events (Treatment Clinical Judgements)					
Of all patients needing treatment,					GC Expert Opinion
percentage who have Cervical Spinal Cord Injury (CSCI)	10%	Uniform	Min =9% , Max =11%		
percentage who do not have CSCI	90%	Uniform	Min = 81%, Max =99%		
Of all patients with CSCI,					
percentage who have complete CSCI ?	50%	Uniform	Min = 45%, Max =55%		
percentage who have partial CSCI	50%	Uniform	Min = 45%, Max =55%		

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Of the patients with complete CSCI,				
percentage who have compression	90%	Uniform	Min = 81%, Max =99%	
percentage who do not have compression	10%	Uniform	Min = 9%, Max =11%	
Of the patients with complete CSCI and compression,				
Percentage who have surgical treatment	90%	Uniform	Min = 81%, Max =99%	
Percentage who have non-surgical treatment	10%	Uniform	Min = 9%, Max =11%	
Of the patients with complete CSCI and no compression,				
percentage who are stable	50%	Uniform	Min = 45%, Max =55%	
percentage who are unstable	50%	Uniform	Min = 45%, Max =55%	
Of the patients with partial CSCI,				
percentage who have compression	50%	Uniform	Min = 45%, Max =55%	
percentage who do not have compression	50%	Uniform	Min = 45%, Max =55%	
Of patients with partial CSCI and compression,				
percentage who have surgical procedure	90%	Uniform	Min = 81%, Max =99%	
percentage who have non-surgical procedure	10%	Uniform	Min = 9%, Max =11%	

Parameter description	Deterministic estimate	Probability distribution	Distribution parameters	Source
Of patients with partial CSCI and no compression,				
percentage who are stable	75%	Uniform	Min = 68%, Max =83%	
percentage who are unstable	25%	Uniform	Min = 23%, Max =28%	
Of patients with no CSCI,				
percentage who are stable?	90.0%	Uniform	Min = 81%, Max =99%	
percentage who are unstable	10.00%	Uniform	Min = 9%, Max =11%	

CSI = Cervical Spine Injury; CT = Computed Tomography; FE = Flexion Extension X-ray; HI = Head Injury; MRI = Magnetic Resonance Imaging; NEXUS = National Emergency X-Radiography Utilisation Study;

H.1.3.2 Resource use and cost

NHS reference costs 2011-2012¹¹ were used to identify cost estimates for diagnostic imaging and treatment for CSI used in the base case analysis. Details are reported below.

Diagnostic Imaging

Diagnostic imaging costs are routinely incorporated in inpatient HRG codes. However, Multiple Trauma HRG codes and Emergency Medicine HRG codes relevant to our population were considered inadequate for our purposes as these cost codes were minimally influenced by differences in diagnostic imaging interventions and were largely derived from surgical and medical procedures.

As a result, unbundled costs for diagnostic imaging were used to allow for clear cost differentiations. The GC judged this to be appropriate especially because a significant proportion the population could have diagnostic imaging without patient admittance into hospital.

The cost of CT and MRI diagnostic imaging techniques were calculated by taking a weighted average of total activities and cost in outpatient, direct access and other settings. The GDG judged that a CT or MRI scan requires a scan of two areas considering patients will need their head and cervical spine areas examined (NHS Reference Cost Codes 2011-2012 RA11Z; RA04Z). The cost of a CT was £104 and the cost of a MRI was £182.

The cost of diagnostic imaging with x-ray (Plain Film Radiograph) was £30.3 and was derived from NHS Reference Costs 2011-2012 cost code DAPF. The GDG judged a flexion extension investigation would require 2 plain film X-rays with a total cost of £61.

Cost of treatment

Costs for treatment were derived from NHS Reference Costs 2011-2012, HC codes (Spinal Surgery and Disorders Chapter). There is a certain degree of double counting as each NHS reference cost code (HC01-HC06) is applied to more than one treatment cost calculation.

This was deemed appropriate as the GC judged procedures within NHS reference codes HC01-HC06 were applicable to multiple treatment categories.

A patient who is discharged upon clinical impressions and diagnostic imaging results showing no abnormality does not require treatment and accrues a cost of £0. The GC judged the cost of discharge to be similar across all patients who remain alive. Thus, the cost of discharge was not considered necessary for our incremental analysis.

Some patients with CSI and in need of treatment are inappropriately discharged and experience deterioration. The GC assumed that a patient who deteriorates will again present to the hospital, undergo diagnostic imaging, and then receive treatment. Assuming a worst-case scenario where the diagnostic investigation requires all types of diagnostic imaging (a CT, MRI, FE X-ray and an X-ray) and the treatment requires a surgical and/or non-surgical procedure, the maximum cost for deterioration is £7,214. Those patients who do not experience deterioration did not accrue any additional costs.

In particular, where a surgical procedure was deemed appropriate, the cost was £7,117, the weighted average of NHS cost codes HC01-HC04. The cost of a non-surgical procedure was £4,459 and was the weighted average of NHS cost codes HC05 and HC06. Using the NHS Reference cost code HC21B weighted across settings, the cost of no procedure with SCI was £17,252 for an average length of stay of 42 days. The cost of a surgical or non-surgical procedure was £6,837 calculated as the weighted average of NHS reference cost codes HC01-HC06. According to the NHS reference cost code HC21C weighted across settings, the cost of no procedure for patients without CSI was £4,979 for an average length of stay of 5.6 days.

H.1.3.3 Diagnostic mark-up

For each strategy, the diagnostic mark-up provides the total cost and number of diagnostic images undertaken per diagnostic technique (X-ray, CT, MRI, and FE X-ray). The total number of diagnostic images was the sum of diagnostic images undertaken at initial and at further imaging stages.

Initial Imaging

The number of patients who received initial imaging (CT, X-ray, or no imaging) was different according to strategy. In blanket Strategies 1-3, the entire cohort received initial CT / X-ray imaging or no imaging. In Strategies 4-7, the number of patients who received initial imaging was determined by the sensitivity and specificity of prediction rules. These strategies did not indicate diagnostic imaging (CT/X-ray) for all patients. For Example, in Strategy 4 (Canadian C-spine for X-ray), the prediction rule did not recommend an X-ray for 58% of patients without CSI. The GDG assumed that these patients might still be imaged. To determine the proportion of patients who would receive the remaining diagnostic imaging alternatives, the GDG estimated half of all remaining patients would receive no imaging and the other half of all remaining patients would receive the alternative diagnostic imaging technique (CT/X-ray). In Strategy 4, the prediction rule did not recommend an X-ray for 58% of patients without CSI and of these 58%, 29% received CT and 29% received no Imaging Details on the GDG estimated apportioning of patients to all initial imaging alternatives for each strategy can be found in Figure 74.

Figure 60

Probability of having a given initial image strategy	Initial clinical decision (for those without injury)			Initial clinical decision (for those with injury)		
	No imaging	CT first	X ray first	No imaging	CT first	X ray first
Strategy 1: No imaging	100%			100%		
Strategy 2: CT all		100%			100%	
Strategy 3: x ray all			100%			100%
Strategy 4: Canadian C spine for Xray	29%	29%	43%	0%	0%	100%
Strategy 5: Canadian C Spine for CT	49.7%	0.6%	49.7%	0%	100%	0%
Strategy 6: NEXUS for Xray	32%	32%	37%	4.65%	4.65%	90.70%
Strategy 7: NEXUS for CT	38%	24%	38%	5%	90%	5%

Further Imaging

The number of further diagnostic imaging performed was determined by the results from the initial diagnostic imaging technique. Results from a diagnostic imaging technique were categorised as normal (diagnostic imaging and clinical impression finds no abnormality), indeterminate (diagnostic imaging and clinical impression finds presence or absence of injury uncertain) or abnormal (abnormality is clear from diagnostic imaging and clinical impression). The number of normal and abnormal results were derived by from the sensitivity (abnormal) and specificity (normal) of diagnostic clearance strategies found in published literature (Halpern 2010) ²⁴. However, there is no data available to inform the number of indeterminate results from diagnostic imaging. The GDG considered that a certain proportion normal and abnormal results would be considered ‘indeterminate’ and that these proportions would differ for a population with CSI and a population without CSI.

Patients who did not receive initial imaging and patients with normal initial imaging results would not be given any further imaging or treatment.

Patients with an indeterminate or abnormal initial imaging result could receive further diagnostic imaging. The type and number of further diagnostic imaging (maximum number = 3) was determined by clinical judgement.

Therefore, the cost of diagnostic imaging was the product of the total number of diagnostic imagings undertaken per diagnostic technique and the unit cost of each diagnostic technique.

Where there is indication of abnormality from diagnostic imaging results and clinical impressions, further management is required.

H.1.3.4 Treatment component

The treatment component uses GDG clinical judgments to subcategorise patients requiring treatment according to injury characteristics so as to identify the type of treatment required and apply the correct weighting to costs. These GDG judgements are detailed in section M.1.2.1. The cost of treatment was calculated as the sum of the cost of each category of treatment. The cost of each category of treatment was the product of the number of treatments and the unit cost of treatment.

H.1.3.5 Computations

The analysis was undertaken using Microsoft Excel 2010. The model is a cohort decision-tree. The PSA was conducted using 7500 simulations (see M.1.4). Each strategy is made up of a diagnostic and treatment component. The prevalence of CSI combined with the performance of prediction rules and the performance of diagnostic imaging techniques

determined the number of patients correctly provided treatment (TP), incorrectly provided treatment (FP), correctly left untreated (TN), and incorrectly left untreated (FN).

For computations informing estimation of cost effectiveness please refer to sections M.1.5 and M.1.6.

H.1.3.6 Sensitivity analyses

A number of deterministic sensitivity analysis were undertaken to investigate uncertain individual input parameters. The GDG wished to identify whether varying that individual input value would have an effect on results. The following inputs were investigated using DSA.

1. Cost of no procedure for patients with and without CSI: there was uncertainty around the cost differentiation for no procedure in patients with (£17,252) and without CSI (£4,979). Hence, the cost for no procedure was made equal for both patients with and without CSI at £ 5,141. This was the weighted cost of HC21B and HC21C across NHS settings for a 10 day length of stay.
2. Litigation cost associated with a FN: given the uncertainty around the average litigation cost for a missed CSI, the litigation cost was varied from £0 to £1,000,000.
3. Initial imaging decisions: there was uncertainty over the base case percentage of patients without CSI who would receive initial imaging (CT/X-ray) or no imaging according to clinical decision rules in Strategies 1-7. Primary analysis percentages were calculated based on the sensitivity and specificity of clinical decision rules and GDG estimates. The uncertainty was attributed to the low quality of specificity data for prediction rules in Duane¹⁵ and Griffith²³. This was explored by calculating percentages using different GDG estimates as indicated in Figure 75 (see percentages highlighted by red rectangle) .
4. QALY pay-offs: in the absence of applicable Quality of Life information for this population, an extremely conservative QALY pay-off was assigned to each outcome (TP, FN, TN, and FP) in a hypothetical scenario. The QALY payoffs assigned (TP = 1.5 QALYs, TN & FP =2 QALYs, and FN = 1 QALY) served to incorporate the smaller pay-off associated with a FN in comparison to patients without CSI (TN) and patients who received treatment (TP and FP). Net monetary benefit was subsequently calculated using Equation 1, where 'Outcome' was equal the number of QALYs and D was equal to the threshold of £20,000 per QALY gained.
5. Prevalence of patients over the age of 16 with CSI: given the absence of information on the prevalence of CSI, the prevalence was varied between 0.5% (base case) to 5% in increments of 0.5%.
6. Clinical decision for further imaging of indeterminate and negative initial imaging results: Given the absence of clinical and economic evidence on the clinical and cost-effectiveness identified for Strategies 1-7 and their application to further imaging scenarios, the following scenarios were compared
 - a. further imaging on indeterminate cases only (base case analysis)
 - b. no further imaging on negative or indeterminate cases
 - c. further imaging on all negative and indeterminate cases

In scenarios a. to c., positive initial imaging results receive further imaging.

Figure 61 GDG estimation of initial imaging probabilities for those without injury (Strategy 4-7)

Probability of having a given initial image strategy	Initial clinical decision (for those without injury)			Initial clinical decision (for those with injury)		
	No imaging	CT first	X ray first	No imaging	CT first	X ray first
7						
Strategy 1: No imaging	100%			100%		
Strategy 2: CT all		100%			100%	
Strategy 3: X ray all			100%			100%
Strategy 4: Canadian C spine for Xray	54%	3%	43%	0%	0%	100%
Strategy 5: Canadian C Spine for CT	54%	46%	0%	0%	100%	0%
Strategy 6: NEXUS for Xray	60%	3%	37%	4.65%	4.65%	90.70%
Strategy 7: NEXUS for CT	22%	40%	38%	5%	90%	5%

Probabilistic Sensitivity Analysis

For the probabilistic analysis, inputs were parameterised with distributions as described in

Table 70 below. To parameterise the reference costs probabilistically, three distributions (gamma, lognormal and normal) were fitted and the best-fit distribution was chosen. Each distribution was fit using the standard deviation of the trust cost (calculated using the reported mean and interquartile range), and where appropriate, the distribution's alpha and beta values. The distribution that provided the interquartile range closest in value to the interquartile range reported by the NHS reference cost was considered the best fit distribution. Estimates from the best-fit distribution were applied to the formulas listed below to calculate the standard error of the mean NHS cost and subsequently, the probabilistic value was drawn.

Table 31: Description of the type and properties of distributions used in the probabilistic sensitivity analysis

Parameter	Probability distribution	Properties of distribution
Clinical Judgements	Uniform	Uniform distribution fitted between the minimum and maximum range allows an equal chance of any value within this range being selected in any simulated run of the probabilistic analysis. The minimum and maximum range for clinical judgements was $\pm 10\%$ of the base case value with a maximum of 100%.
Performance of prediction rules (sensitivity and specificity)	Beta	Beta distribution fitted between 0 and 1. As the sample size and the number of events were specified alpha and beta values were calculated as follows: Alpha: (number of patients with CSI/without CSI) Beta=(Number of patients)-(number of patients with CSI/without CSI)
Performance of diagnostic imaging techniques (sensitivity and specificity)	Beta	Beta distribution fitted between 0 and 1. Derived from mean of a domain or total quality of life score and its standard error, using the method of moments. Alpha and Beta values were calculated as follows: Alpha = $mean^2 * (1 - (mean/SE)^2) - mean$ Beta = $Alpha * ((1 - mean)/mean)$
Number of indeterminate results after imaging technique	Beta	Beta distribution fitted between 0 and 1. The sample size and the number of events were specified by the cohort size and GDG estimations. Thus, alpha and beta values were calculated as follows: Alpha = (number of patients with indeterminate result) Beta = (Number of patients)-(number of patients with indeterminate results)
NHS Reference Costs (diagnostic and treatment)	Gamma	Gamma distribution bounded at 0 and positively skewed. Derived from mean and its standard error. Alpha and Beta values were calculated as follows: Alpha = $(mean/SE)^2$ Beta = $SE^2/Mean$
NHS Reference Costs (diagnostic and treatment)	Lognormal	Where appropriate, the lognormal distribution may provide a better fit than the gamma distribution for costs. The natural log of the mean was calculated as follows: Natural log of the mean = $[Ln(mean) - (lnSE)^2]/2$ Where the natural log of the standard error (lnSE) was calculated by: $\sqrt{\ln \frac{SE^2 + mean^2}{mean^2}}$
NHS Reference Costs (diagnostic and treatment)	Normal	Where appropriate, the normal distribution may provide a better first than the gamma and lognormal distribution for costs. The mean and standard error was calculated as follows: Mean = $\frac{sum\ of\ all\ values}{number\ of\ values}$ Standard Error = $\frac{standard\ deviation}{\sqrt{number\ of\ values}}$

With all distributions drawn, a simulation was run for each strategy independently and key results of each simulation were copied and stored. To compare the results generated for a single iteration, the starting seed for each random number selected for the probabilistic analysis was reset to original with each rerun of the probabilistic simulation. This assured, for example, the PSA referred to the same prevalence for all seven strategies in any given iteration and ensured the results for each iteration across the strategies were comparable.

H.1.4 Estimation of cost effectiveness

The widely used cost-effectiveness metric is the incremental cost-effectiveness ratio (ICER). This is calculated by dividing the difference in costs associated with two alternatives by the difference in QALYs. The decision rule then applied is that if the ICER falls below a given cost per QALY threshold the result is considered to be cost effective. If both costs are lower and QALYs are higher the option is said to dominate and an ICER is not calculated.

$ICER = \frac{Costs(B) - Costs(A)}{QALYs(B) - QALYs(A)}$ <p>Where: Costs/QALYs(X) = total costs/QALYs for option X</p>	<ul style="list-style-type: none"> • Cost-effective if: ICER < Threshold
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When there are more than two comparators, as in this analysis, options must be ranked in order of increasing cost then options ruled out by dominance or extended dominance before calculating ICERs excluding these options. An option is said to be dominated, and ruled out, if another intervention is less costly and more effective. An option is said to be extendedly dominated if a combination of two other options would prove to be less costly and more effective.

It is also possible, for a particular cost-effectiveness threshold, to re-express cost-effectiveness results in term of net monetary benefit (NMB). This is calculated by multiplying the total QALYs for a comparator by the threshold cost per QALY value (for example, £20,000) and then subtracting the total costs (formula below). The decision rule then applied is that the comparator with the highest NMB is the most cost-effective option at the specified threshold. That is the option that provides the highest number of QALYs at an acceptable cost.

$NMB(X) = (QALYs(X) \times \lambda) - Costs(X)$ <p>Where: NMB= Net Monetary Benefit; Costs/QALYs(X) = total costs/QALYs for option X; λ = threshold</p>	<ul style="list-style-type: none"> • Cost-effective if: highest net monetary benefit
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Both methods of determining cost effectiveness will identify exactly the same optimal strategy. For ease of computation, adaptations of the NMB formula are used in this analysis to identify the optimal strategy.

In the case of cost-effectiveness analysis where cost per QALY is not estimated, and rather an alternative outcome (i.e. cost per false negative avoided) is used, there is not a specific cost per effect threshold employed to assess cost effectiveness. However, these outcomes can still be used to identify dominated and extendedly dominated options. Further, an assumed cost and/or QALY weight can be attached to such outcomes to enable net monetary benefit calculations, as described in the below equations:

$NMB(X) = (Outcome(X) \times QALY_Weight \times \lambda) - Costs(X)$ <p>Where: NMB = Net Monetary benefit; Outcome(x) = the diagnostic outcome for which the QALY weight applies; λ = threshold of £20,000</p>	<ul style="list-style-type: none"> • Cost-effective if: highest net monetary benefit
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$$NMB(X) = (FN(X) \times -LitigationCost) - Costs(X)$$

Where: NMB = Net Monetary Benefit; FN = False negatives identified; litigation costs represents the negative cost associated with the false negative and Costs (x) is the total cost of the strategy

- Cost-effective if: highest net monetary benefit

H.1.4.1 Interpreting results

NICE's report 'Social value judgements: principles for the development of NICE guidance' sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- The intervention costs less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

In the absence of data to inform a lifetime costs and QALYs associated with the strategies (i.e. data on longterm survival and medical events), the model evaluates the diagnostic strategies using three types of analyses, each referencing a different key outcome. These are:

- a) A cost effectiveness analysis which compares the cost per false negative avoided in a given strategy.
- b) A cost minimisation analysis whereby the litigation costs accrued are evaluated against the cost of the strategy, with results expressed in net monetary benefit.
- c) A simplistic cost utility sensitivity analysis which compares the net monetary benefit associated with each strategy given minimal QALY gains per correct diagnosis and minimal QALY loss per incorrect diagnosis.

As we have several strategies of comparison, we use Net Monetary Benefit to rank the strategies on the basis of their relative cost-effectiveness and identify dominated or extendly dominated options.

A note on Net Monetary Benefit Analysis using litigation costs.

Using information on total cost and outcome and assuming the litigation cost penalty associated with a FN was -£200,000, net monetary benefit was calculated. This statistic was calculated as the number of False Negatives multiplied by the cost penalty (a litigation penalty of -£200,000) minus the total cost of strategy (Equation 1). Because the cost penalty of a false negative was greater than the total cost of strategy, the net monetary benefit figure is negative. Net Monetary Benefit Results were ranked from 1 to 7 across all strategies with Rank 1 representing the largest Net Monetary Benefit and Rank 7 as the least Net Monetary Benefit.

To minimise costs, the GDG would consider the strategy with the highest net monetary benefit. In the sensitivity analysis where QALYs were assigned to each outcome, the monetary value associated with each QALY gained was £20,000. The GDG would consider the optimal or dominant strategy from this analysis when making recommendations.

H.1.4.2 Model validation

The model was developed in consultation with the GC; model structure, inputs and results were presented to and discussed with the GC for clinical validation and interpretation.

The model was systematically checked by the health economist undertaking the analysis; this included inputting null and extreme values and checking that results were plausible given inputs. The model was peer reviewed externally and by a second experienced health economist from NICE; this included systematic checking of the model calculations.

H.2 Results

H.2.1 Base Case Results

Each strategy is composed of diagnostic imaging, outcomes, and treatments. Thus, **Table 71** - **Table 74** qualify the differences in base case deterministic diagnostic imagings, outcomes and treatments across strategies. Understanding these differences will help the interpretation of base case probabilistic results in **Table 75** and **Table 76**.

Table 71 presents a breakdown of the total number of diagnostic imaging according to the strategy. The table also shows the percentage of the cohort who receives each type of diagnostic imaging.

Table 72 presents a breakdown of the performance of each strategy. Outcomes are considered as the percentage of TP, FN, TN and FP. In each strategy, majority of patients without CSI are correctly diagnosed as TN and very few are incorrectly diagnosed as FP. A significant proportion of patients with CSI are incorrectly diagnosed as FN. The strategy with the smallest (28%) and largest (100%) percentage of FNs are Strategy 2/Strategy 5 (CT for all/Canadian C-spine for CT) and Strategy 1 (No Imaging) respectively.

As **Table 73** illustrates, very few patients are treated across strategies. At the extremes, no one is treated in Strategy 1 (No Imaging) and 7 patients out of 1,000 are treated in Strategy 5 (Canadian C-spine for CT). Of those who receive treatment, the majority do not receive a procedure but are instead observed in hospitals (those who are given no procedure with or without CSI).

Table 74 presents the total cost of each strategy. Strategy 3 (X-ray all) is most costly while Strategy 1 (No Imaging) is least costly. The cost of each strategy is most influenced by the cost of diagnostic imaging and the cost of observation. Because of the small number of patients treated across strategies, the cost of treatment assumes a relatively small proportion of the total cost of strategy. By considering both the number of diagnostic imaging results as well as the differential cost across types of diagnostic imaging, the total costs of each strategy is calculated. The strategies with the highest (£289,558) and lowest (£0) diagnostic imaging costs are Strategy 2 (CT all) and Strategy 1 (No Imaging) respectively.

The Net Monetary Benefit analysis (**Table 75**) provides the base case deterministic results and illustrates that Strategy 5 (Canadian C-spine for CT) is the optimal strategy (highest net monetary benefit) while Strategy 1 (No Imaging) was the least optimal (lowest net monetary benefit).

In addition, **Table 76** presents the results of the cost effectiveness analysis where incremental costs and false negatives avoided were calculated using Strategy 1 (No Imaging) as the base comparator. The lowest (£88,458) and highest (£271,310) costs per false negative avoided were associated with Strategy 5 (Canadian C-Spine for CT) and Strategy 3 (X-ray on all) respectively.

H.2.2 Sensitivity Analysis Results

Strategy 5 remained the optimal strategy in the probabilistic analysis, and it was the most cost-effective strategy in 93% of the simulations. Strategy 5 was optimal despite variation to

individual inputs - equal costs for no procedure with or without CSI (Table 76); GDG estimated initial imaging decisions (Table 78); QALY pay-offs (Table 79); prevalence of CSI between 0.5%-5% (Figure 76) in the deterministic sensitivity analysis. Assuming that Strategy 1 (No Imaging) is not an ethical option, Strategy 5 was also the optimal strategy when the litigation costs associated with a missed FN was between £0 and £1,000,000 (Table 77). Strategy 5 was also the optimal strategy when the clinical decision was to not further image normal and indeterminate results or to only further image indeterminate results. When the clinical decision was to further image both normal and indeterminate results, Strategy 2 (CT all) became optimal.

In the sensitivity analysis that assigned a minimal QALY advantage per correct diagnosis it was found that no imaging ranked optimal. If no imaging was not considered an acceptable or ethical strategy, then strategy 5 would be the most optimal strategy.

H.3 Interpreting results

H.3.1 Summary of results

The probabilistic analysis identified Strategy 5 (Canadian C-spine for CT) to be dominant at a threshold of £200,000 for each FP outcome meaning that Strategy 5 was less costly and avoided more FPs than all the other strategies. Strategy 5 also had the lowest cost per False Negative avoided. This conclusion was robust to variations in the prevalence of CSI (0.5%-5%), cost of no procedure with or without CSI and GDG estimated initial imaging decisions and when the decision to not further image or to further image only indeterminate results. When the clinical decision was to further image both normal and indeterminate results, the optimal strategy changed to Strategy 2 (CT all).

The results were sensitive to the cost of litigation associated with a false negative, with the optimal ranking switching from no imaging to strategy 5 when litigation costs rose from £75,000 to £100,000. No imaging was also seen as an optimal strategy if only a minimal QALY advantage was associated with achieving a true positive in comparison to other diagnostic outcomes. Strategy 5 was the next optimal strategy in this analysis.

H.3.2 Limitations and interpretation

We acknowledge the CEA does not fully account or quantify all the trade offs involved with the diagnostic decision question, as no weighting or penalty was given to other diagnostic outcomes such as false positives (although unnecessary treatment cost is taken into account). However, the estimated negative monetary payoff of £200,000 associated with each FN outcome implicitly took into account the adverse effects of radiation and the potential of deterioration after treatment or no treatment. Nonetheless, it is necessary to interpret this analysis with caution as it has some potentially serious limitations.

That the 'No Imaging' strategy may be optimal in scenarios where there are limited negative consequences associated with a false negative finding and where there is little to gain with positive findings (i.e. correct onward treatment and QALY gain) is a reflection of the low prevalence of CSI within a head injury population and the trade off involved with the decision problem. A low prevalence of a condition will inevitably lower the negative predictive values of a diagnostic intervention (in comparison to if the diagnostic intervention was placed in a high prevalence setting), an in turn favour a non-imaging strategy, especially when the downstream consequences of a correct or incorrect diagnostic are marginal in relation to each other. In this model, an extremely conservative estimate of the gains of diagnostics was specified.

The GC felt that despite the limitations, the analysis is sufficiently robust for purposes of decision-making as it explicitly shows and attempts to quantify the parameters, assumptions

and structure underpinning the decision. To interpret the results, the GC acknowledged that the consequences of each diagnostic outcome was uncertain, and took the view that in practice a non imaging strategy was not viable to recommend.

Assuming that Strategy 1 (No Imaging) was a theoretical strategy not plausible (ethical) in practice, the CT according to Canadian C-spine was optimal when the false negative litigation costs varied from £0 - £1,000,000. The conclusion that CT using the Canadian C-spine prediction rule remained gave the greatest net monetary benefit in the scenario of minimal QALY gain associated with each true positive and minimal QALY loss with each false negative under the assumption that No Imaging was not appropriate in practice.

With the view that a non-imaging strategy could not be recommended, the sensitivity analysis whereby an extremely conservative scenario was explored in terms of pay-off indicates that despite the limitations of the CEA, the conclusions formed by the analysis appear robust. In addition, that Strategy 5 (CT according to Canadian C-spine) remained robust when the threshold value associated with a FN was varied from £0 to £1,000,000 (assuming the No Imaging strategy was not appropriate in practice) also supports the conclusions made in this analysis. In line with the NICE reference case, all parameters subject to uncertainty (i.e. unit costs, sensitivities and specificities of the prediction rules and clinician estimates) were parameterised probabilistically and probabilistic sensitivity analysis performed.

H.3.3 Generalisability to other populations

A separate subgroup analysis was not conducted for a paediatric population. The results of this analysis are not applicable for children under the age of 16 with HI and suspected CSI. The GC felt this economic analysis could not be extrapolated to the paediatric population as this is clinically quite different from the adult population. No evidence was identified for paediatrics and so, it was not possible to determine the appropriateness of model inputs for the paediatric population (in particular, the prevalence of CSI & the clinical judgements for further imaging and treatment used in the analysis for adults). For this population, the trade-off between the accuracy of diagnosis and the radiation risk associated with a CT scan (equivalent to 2 years background radiation) requires particular discussion. The GC would consider that a plain film X-ray has lower levels of radiation than a CT scan when writing recommendations for children.

H.3.4 Comparisons with published studies

No studies that looked at the use of prediction rules for the selection of HI patients with suspected CSI for diagnostic imaging were identified. One study by Pandor et al 2011,379 which investigated the use of prediction rules for the management of patients with minor HI found that in comparison to 9 other strategies, the Canadian CT Head Rule (CCHR) medium and high-risk prediction rule was the most cost-effective. Given this conclusion, the GC considered that the CCHR could be used for a patient with HI and suspected CSI to rule out HI. Then, according to the conclusions from this analysis, Canadian CT Spine rule could be used for the same patient to rule out suspected CSI.

H.3.5 Conclusion

For patients with HI and suspected CSI, the Canadian C-spine decision rule is cost-effective for selecting patients for diagnostic imaging.

H.3.6 Implications for future research

The time horizon of this analysis only extended to the end of treatment. Considering this short time horizon and exclusion of quality-of-life health outcomes in this analysis, future research could explore the costs and health outcomes for a lifetime horizon. Results from this analysis were not extrapolated to the patient subgroup under the age of 16 because of a

dearth of available information. Should clinical studies that look at the accuracy of prediction rules for children be available in the future, this analysis can be modified to provide information on the cost-effectiveness of C-spine injury clearance strategies for this subgroup.

H.4 Additional Tables and Figures

Base Case Results

Table 32 : Base Case Deterministic Analysis— Breakdown of Diagnostic Imaging for each Strategy

Base case Breakdown of Diagnostic Imaging for each strategy (prevalence 0.5%, cohort N = 1000)				
Strategy	# of Xrays (%)	# of CTs(%)	# of MRIs(%)	# of FE X-rays(%)
Strategy 1: No imaging	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Strategy 2: CT all	0 (0%)	1000 (100%)	751 (75%)	812 (82%)
Strategy 3: X-ray all	1000 (100%)	792 (80%)	602 (61%)	643 (65%)
Strategy 4: Canadian C-spine for X-ray	433(43%)	626 (63%)	473 (48%)	508 (51%)
Strategy 5: Canadian C-spine for CT	495 (50%)	403 (40%)	307 (31%)	326 (33%)
Strategy 6: NEXUS for X-ray	371 (37%)	608 (61%)	459 (46%)	493 (50%)
Strategy 7: NEXUS for CT	379 (38%)	542 (54%)	410 (41%)	439 (44%)

Table 33: Base Case Deterministic Analysis – Performance of Strategies

Base case Results: Performance of Strategy (prevalence 0.5%, cohort N = 1000)				
Strategy	patients without CSI		patients with CSI	
	% True Negative	% False Positive	%False Negative	%True Positive
Strategy 1: No imaging	100.0%	0.0%	100%	0%
Strategy 2: CT all	99.7%	0.3%	28%	72%
Strategy 3: X-ray all	99.7%	0.3%	56%	44%
Strategy 4: Canadian C-spine for X-ray	99.8%	0.2%	56%	44%
Strategy 5: Canadian C-spine for CT	99.8%	0.1%	28%	72%
Strategy 6: NEXUS for X-ray	99.8%	0.2%	57%	43%
Strategy 7: NEXUS for CT	99.8%	0.2%	33%	67%

Table 34: Base Case Deterministic Analysis – Breakdown of Treatment Types

Base case Results: Breakdown of Types of Treatment (prevalence 0.5%, cohort N = 1000)						
Strategy	# of T* using surgical procedures only	# of T* using non surgical procedures only	# of T* where surgical or non surgical treatment is possible	#of T* with CSCI using no procedure ¹	# of T* without CSCI using no procedure ²	Total # Treated
Strategy 1: No imaging	-	-	-	-	-	0.0
Strategy 2: CT all	0.4	0.0	0.7	0.1	5.5	6.8
Strategy 3: X-ray all	0.3	0.0	0.5	0.1	3.9	4.8
Strategy 4: Canadian C-spine for X-ray	0.3	0.0	0.4	0.1	3.4	4.2
Strategy 5: Canadian C-spine for CT	0.3	0.0	0.5	0.1	4.0	4.9
Strategy 6: NEXUS for X-ray	0.3	0.0	0.4	0.1	3.3	4.1
Strategy 7: NEXUS for CT	0.3	0.0	0.5	0.1	4.1	5.1

T* = treatments

¹ = Number of patients with CSCI where diagnostic result indicates the need for treatment but injury characteristics indicate that no surgical or non surgical procedure is beneficial. Thus, no procedure is provided.

² = Number of patients without CSCI where diagnostic result indicates the need for treatment but injury characteristics indicate that no surgical or non surgical procedure is beneficial. Thus, no procedure is provided.

Table 35: Base Case Deterministic Analysis – Breakdown of Cost of Strategy

Base case Breakdown of Costs of Strategy (prevalence 0.5%, cohort N = 1000)				
Strategy	Cost of Treatment	Cost of Diagnostic Imaging	Cost of Observation	Total Cost of Strategy
Strategy 1: No imaging	£-	£-	£1,245	£1,245
Strategy 2: CT all	£37,930	£289,558	£1,264	£328,753
Strategy 3: X-ray all	£26,547	£260,916	£270,549	£558,012
Strategy 4: Canadian C-spine for X-ray	£23,496	£194,888	£117,019	£335,403
Strategy 5: Canadian C-spine for CT	£27,151	£132,283	£135,132	£294,566
Strategy 6: NEXUS for X-ray	£22,957	£187,678	£100,324	£310,960
Strategy 7: NEXUS for CT	£28,313	£168,905	£103,883	£301,102

Table 36: Base Case Deterministic Analysis Results with Probabilistic Analysis Rank

Base Case Deterministic Analysis CEA Results (prevalence 0.5%, cohort N = 1000)					
Strategy	Total Cost of Strategy	Total # of False Negatives Identified	Net Monetary Benefit	Rank	% ranked in PSA
Strategy 1: No imaging	£1,245	5.00	-£1,001,245	6	0%
Strategy 2: CT all	£328,753	1.42	-£612,099	2	7%
Strategy 3: X-ray all	£558,012	2.79	-£1,116,022	7	0%
Strategy 4: Canadian C-spine for X-ray	£335,403	2.79	-£893,413	5	0%
Strategy 5: Canadian C-spine for CT	£294,566	1.42	-£577,912	1	93%
Strategy 6: NEXUS for X-ray	£310,960	2.83	-£876,751	4	0%
Strategy 7: NEXUS for CT	£301,102	1.66	-£633,022	3	0%

Table 37: Base Case Probabilistic Analysis—Cost per False Negative Avoided

Base Case Probabilistic Results (prevalence 0.5%, cohort N = 1000)						
Strategy	Total Cost of Strategy	Incremental Cost of Strategy	Total # of FN Identified	Incremental # of FN Avoided	Net Benefit	Incremental Cost per False Negative Avoided
Strategy 1: No imaging (reference)	£1,214	-	5.00	-	-£1,000,947	-
Strategy 2: CT all	£328,041	£326,828	1.69	3.31	-£665,914	£98,760
Strategy 3: x ray all	£556,884	£555,670	2.95	2.05	-£1,146,996	£271,310
Strategy 4: Canadian C spine for Xray	£333,997	£332,783	2.95	2.05	-£924,109	£162,483
Strategy 5: Canadian C Spine for CT	£293,948	£292,734	1.69	3.31	-£631,821	£88,458
Strategy 6: NEXUS for Xray	£310,297	£309,083	2.99	2.01	-£907,807	£153,875
Strategy 7: NEXUS for CT	£300,537	£299,324	1.91	3.09	-£683,070	£96,994

Deterministic Sensitivity Analyses Results

Table 38: DSA with Cost for No Procedure with or without CSI Equal

Deterministic Sensitivity Analysis on Costs for no procedure with and without CSI (prevalence 0.5%, cohort N = 1000, Equal cost for no procedure with and without CSI)				
Strategy	Total Cost of Strategy	Total # of False Negatives identified	Net Monetary Benefit	Rank
Strategy 1: No imaging	£1,285	5.0	-£1,001,285	6
Strategy 2: CT all	£327,933	1.4	-£611,278	2
Strategy 3: X-ray all	£566,211	2.8	-£1,124,221	7
Strategy 4: Canadian C-spine for X-ray	£338,677	2.8	-£896,687	5
Strategy 5: Canadian C-spine for CT	£298,346	1.4	-£581,692	1
Strategy 6: NEXUS for X-ray	£313,702	2.8	-£879,493	4
Strategy 7: NEXUS for CT	£303,838	1.7	-£635,759	3

Table 39 DSA with Litigation Costs (£0 - £1,000,000)

Deterministic Sensitivity Analysis on Litigation costs (£0-£1,000,000) ; Prevalence of CSI 0.5%; Cohort N =1000												
Strategy	Litigation Cost											
	£0	£25,000	£50,000	£75,000	£100,000	£125,000	£150,000	£175,000	£200,000	£225,000	£250,000	£1,000,000
Strategy 1: No imaging	-£1,245	-	-	-	-	-	-	-£876,245	-	-	-	-
		£126,245	£251,245	£376,245	£501,245	£626,245	£751,245		£1,001,245	£1,126,245	£1,251,245	£5,001,245
Strategy 2: CT all	-	-	-	-	-	-	-	-£576,680	-£612,099	-£647,517	-£682,935	-
	£328,753	£364,171	£399,589	£435,008	£470,426	£505,844	£541,262					£1,745,482
Strategy 3: X-ray all	-	-	-	-	-	-	-	-£1,046,271	-	-	-	-
	£558,012	£627,763	£697,514	£767,266	£837,017	£906,768	£976,520		£1,116,022	£1,185,774	£1,255,525	£3,348,064
Strategy 4: Canadian C-spine for X-ray	-	-	-	-	-	-	-	-£823,662	-£893,413	-£963,165	-	-
	£335,403	£405,154	£474,906	£544,657	£614,408	£684,160	£753,911				£1,032,916	£3,125,455
Strategy 5: Canadian C-spine for CT	-	-	-	-	-	-	-	-£542,494	-£577,912	-£613,330	-£648,748	-
	£294,566	£329,984	£365,402	£400,821	£436,239	£471,657	£507,075					£1,711,295
Strategy 6: NEXUS for X-ray	-	-	-	-	-	-	-	-£806,027	-£876,751	-£947,475	-	-
	£310,960	£381,684	£452,407	£523,131	£593,855	£664,579	£735,303				£1,018,198	£3,139,915
Strategy 7: NEXUS for CT	-	-	-	-	-	-	-	-£591,532	-£633,022	-£674,512	-£716,002	-
	£301,102	£342,592	£384,082	£425,572	£467,062	£508,552	£550,042					£1,960,704

Table 40: DSA with GDG estimates for initial imaging decisions

Base case CEA Results (prevalence 0.5%, cohort N = 1000, prediction rule performance according to GDG estimates)				
Strategy	Total Cost of Strategy	Total # of False Negatives identified	Net Monetary Benefit	Rank
Strategy 1: No imaging	£1,245	5.0	-£1,001,245	6
Strategy 2: CT all	£328,753	1.4	-£612,099	2
Strategy 3: X-ray all	£558,012	2.8	-£1,116,022	7
Strategy 4: Canadian C-spine for X-ray	£335,403	2.8	-£893,413	5
Strategy 5: Canadian C-spine for CT	£294,566	1.4	-£577,912	1
Strategy 6: NEXUS for X-ray	£310,960	2.8	-£876,751	4
Strategy 7: NEXUS for CT	£301,102	1.7	-£633,022	3

Table 41 : DSA using QALY pay-offs (per cohort of 1000 patients)

	QALYs from TP ¹	QALYs from FN ²	QALYs from TN ³	QALYs from FP ⁴	Total QALY	NMB (£20K)	Rank
Strategy 1: No imaging	0.00	5.00	1990.00	0.00	1,995.00	£39,898,755	1
Strategy 2: CT all	5.37	1.42	1983.51	6.49	1,996.79	£39,607,080	4
Strategy 3: X-ray all	3.29	2.79	1983.42	5.17	1,994.67	£39,335,356	7
Strategy 4: Canadian C-spine for X-ray	3.29	2.79	1985.32	4.07	1,995.47	£39,574,054	6
Strategy 5: Canadian C-spine for CT	5.37	1.42	1986.69	2.61	1,996.09	£39,627,239	2
Strategy 6: NEXUS for X-ray	3.23	2.83	1985.53	3.95	1,995.54	£39,599,905	5
Strategy 7: NEXUS for CT	5.01	1.66	1985.95	3.52	1,996.13	£39,621,524	3

¹ QALYs from TP = # of TP multiplied by 1.5 QALYs

² QALYs from FP = # of FP multiplied by 1 QALY

³ QALYs from TN = # of TN multiplied by 2 QALYs

⁴ QALYs from FP = # of FP multiplied by 2 QALYs

1 **Figure 62 DSA with Prevalence of CSI ranging between 0.5%-5% (Cohort N =1000)**

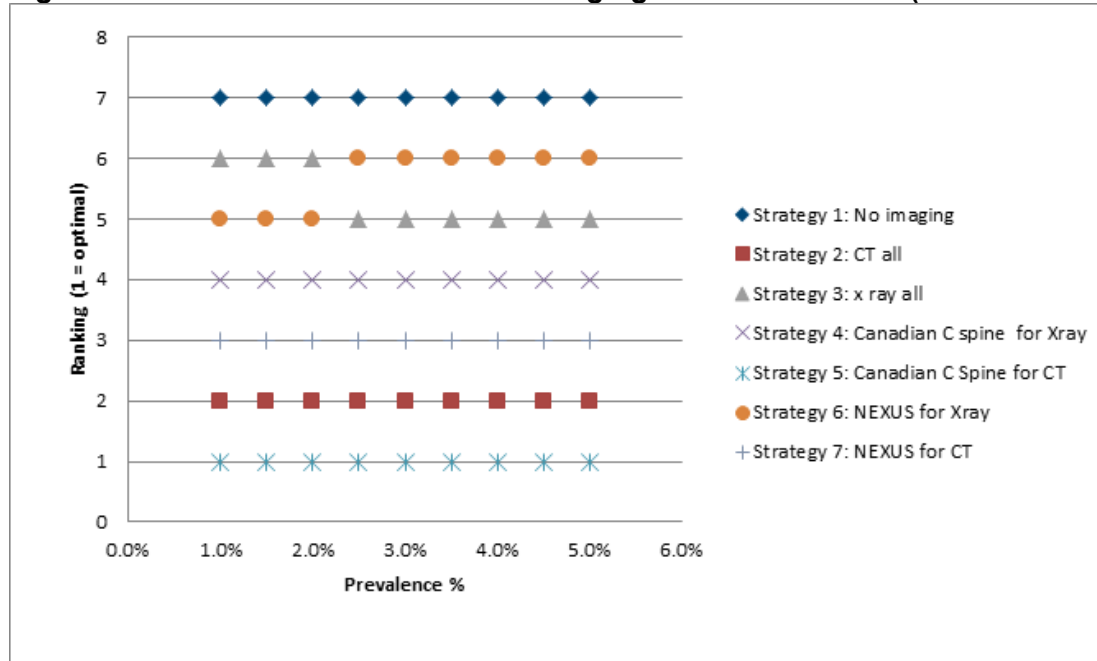
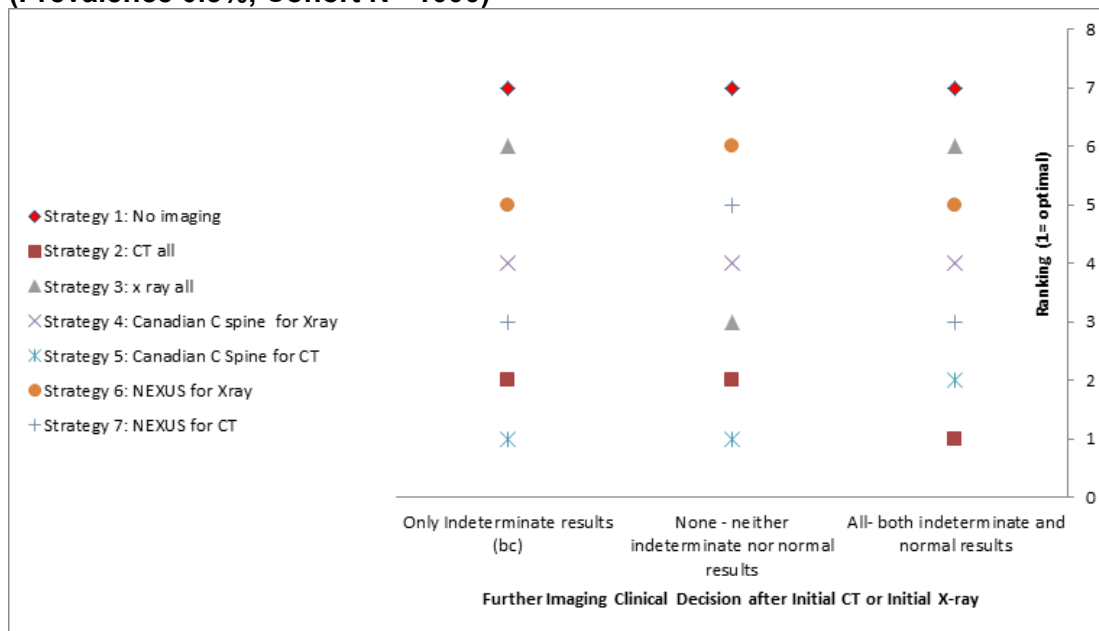


Figure 63 DSA with Further Imaging Clinical Decision Scenarios after Initial CT/X-ray (Prevalence 0.5%, Cohort N =1000)



Appendix I – Excluded studies

Clinical studies

Table 42: Studies excluded from the clinical review

Study	Code [Reason]
Albrecht RM, Kingsley D, Schermer CR et al. (2001) Evaluation of cervical spine in intensive care patients following blunt trauma. World journal of surgery 25(8): 1089-1096	- Study design - not diagnostic accuracy or test and treat
Anekstein, Y., Jeroukhimov, I., Bar-Ziv, Y. et al. (2008) The use of dynamic CT surview for cervical spine clearance in comatose trauma patients: a pilot prospective study. Injury 39(3): 339-46	- Study design - not diagnostic accuracy or test and treat
Antevil, J. L., Sise, M. J., Sack, D. I. et al. (2006) Spiral computed tomography for the initial evaluation of spine trauma: A new standard of care?. J Trauma 61(2): 382-7	- Not specifically cervical spine injury
Arbuthnot, Mary and Mooney, David P (2017) The sensitivity and negative predictive value of a pediatric cervical spine clearance algorithm that minimizes computerized tomography. Journal of pediatric surgery 52(1): 130-135	- Diagnostic test not relevant to review protocol
Awan, O., Safdar, N. M., Siddiqui, K. M. et al. (2011) Detection of cervical spine fracture on computed radiography images a monitor resolution study. Acad Radiol 18(3): 353-8	- Diagnostic test not relevant to review protocol
Bach CM, Steingruber IE, Peer S et al. (2001) Radiographic evaluation of cervical spine trauma. Plain radiography and conventional tomography versus computed tomography. Archives of orthopaedic and trauma surgery 121(7): 385-387	- Study design - only included those with injury already confirmed either on test or reference standard
Badhiwala, Jetan H, Lai, Chung K, Alhazzani, Waleed et al. (2015) Cervical spine clearance in obtunded patients after blunt traumatic injury: a systematic review. Annals of internal medicine 162(6): 429-37	- Study design - all were CT negative to be included
Berritto, Daniela, Pinto, Antonio, Michelin, Paul et al. (2017) Trauma Imaging of the Acute Cervical Spine. Seminars in musculoskeletal radiology 21(3): 184-198	- Review article but not a systematic review

Study	Code [Reason]
Bolinger, B.; Shartz, M.; Marion, D. (2004) Bedside fluoroscopic flexion and extension cervical spine radiographs for clearance of the cervical spine in comatose trauma patients. J Trauma 56(1): 132-6	- Study design - all were CT negative to be included
Brichko, Lisa, Giddey, Birinder, Tee, Jin et al. (2018) Cervical spine traumatic epidural haematomas: Incidence and characteristics. Emergency medicine Australasia : EMA 30(3): 359-365	- Study design - not diagnostic accuracy or test and treat
Brinckman, M.A.; Chau, C.; Ross, J.S. (2015) Marrow edema variability in acute spine fractures. Spine Journal 15(3): 454-460	- Diagnostic test not relevant to review protocol - Study design - only included those with injury already confirmed either on test or reference standard
Brown, C. V., Antevil, J. L., Sise, M. J. et al. (2005) Spiral computed tomography for the diagnosis of cervical, thoracic, and lumbar spine fractures: its time has come. J Trauma 58(5): 890-5; discussion 895	- Study design - only included those with injury already confirmed either on test or reference standard
Brown, C.V.R.; Foulkrod, K.H.; Reifsnnyder, A. (2010) Computed Tomography versus Magnetic Resonance Imaging for Evaluation of the Cervical Spine: How Many Slices do you Need?. The American Surgeon 76(4): 365-368	- Insufficient information to calculate diagnostic accuracy measures
Carter, A.W., Jacups, S.P., Ackland, H.M. et al. (2017) Spinal clearance practices at a regional Australian hospital: A window to major trauma management performance outside metropolitan trauma centres. Journal of Emergency Medicine, Trauma and Acute Care 2017(1)	- Study design - not diagnostic accuracy or test and treat
Chew, Brandon G, Swartz, Christopher, Quigley, Matthew R et al. (2013) Cervical spine clearance in the traumatically injured patient: is multidetector CT scanning sufficient alone? Clinical article. Journal of neurosurgery. Spine 19(5): 576-81	- Study design - not diagnostic accuracy or test and treat - Study design - all were CT negative to be included
Chilvers, G; Janjua, U; Choudhary, S (2017) Blunt cervical spine injury in adult polytrauma: incidence, injury patterns and predictors of significant ligament injury on CT. Clinical radiology 72(11): 907-914	- Study design - not diagnostic accuracy or test and treat

Study	Code [Reason]
<p>Chiu, Ryan G, Siddiqui, Neha, Rosinski, Clayton L et al. (2020) Effect of Magnetic Resonance Imaging on Surgical Approach and Outcomes in the Management of Subaxial Cervical Fractures. <i>World neurosurgery</i> 138: e169-e176</p>	<p>- Study design - only included those with injury already confirmed either on test or reference standard</p> <p>- Study design - not diagnostic accuracy or test and treat</p>
<p>Como, J. J., Leukhardt, W. H., Anderson, J. S. et al. (2011) Computed tomography alone may clear the cervical spine in obtunded blunt trauma patients: a prospective evaluation of a revised protocol. <i>J Trauma</i> 70(2): 345-9; discussion 349</p>	<p>- Study design - all were CT negative to be included</p>
<p>Como, J. J., Thompson, M. A., Anderson, J. S. et al. (2007) Is magnetic resonance imaging essential in clearing the cervical spine in obtunded patients with blunt trauma?. <i>J Trauma</i> 63(3): 544-9</p>	<p>- Full text paper not available</p>
<p>Cui, Li W, Probst, Marc A, Hoffman, Jerome R et al. (2016) Sensitivity of plain radiography for pediatric cervical spine injury. <i>Emergency radiology</i> 23(5): 443-8</p>	<p>- Study design - only included those with injury already confirmed either on test or reference standard</p>
<p>Davies, J; Cross, S; Evanson, J (2016) Radiological assessment of paediatric cervical spine injury in blunt trauma: the potential impact of new NICE guidelines on the use of CT. <i>Clinical radiology</i> 71(9): 844-53</p>	<p>- Diagnostic test not relevant to review protocol</p>
<p>Davis JW, Kaups KL, Cunningham MA et al. (2001) Routine evaluation of the cervical spine in head-injured patients with dynamic fluoroscopy: a reappraisal. <i>The Journal of trauma</i> 50(6): 1044-1047</p>	<p>- Diagnostic test not relevant to review protocol</p>
<p>Diaz JJ, Gillman C, Morris JA et al. (2003) Are five-view plain films of the cervical spine unreliable? A prospective evaluation in blunt trauma patients with altered mental status. <i>The Journal of trauma</i> 55(4): 658</p>	<p>- Reference standard test not relevant to protocol</p>
<p>Diaz, J. J., Jr., Aulino, J. M., Collier, B. et al. (2005) The early work-up for isolated ligamentous injury of the cervical spine: does computed tomography scan have a role?. <i>J Trauma</i> 59(4): 897-903; discussion 903</p>	<p>- Study design - all were CT negative to be included</p>

Study	Code [Reason]
Duane, T. M., Scarcella, N., Cross, J. et al. (2010) Do flexion extension plain films facilitate treatment after trauma?. <i>Am Surg</i> 76(12): 1351-4	- Reference standard test not relevant to protocol
El Saman, Andre, Laurer, Helmut, Maier, Bernd et al. (2007) Diagnosis, Timing and Treatment of Cervical Spine Injuries in Polytraumatized Patients. <i>European journal of trauma and emergency surgery : official publication of the European Trauma Society</i> 33(5): 501-11	- Study design - not diagnostic accuracy or test and treat - Study design - only included those with injury already confirmed either on test or reference standard
Ertel, Audrey E; Robinson, Bryce R H; Eckman, Mark H (2016) Cost-effectiveness of cervical spine clearance interventions with litigation and long-term-care implications in obtunded adult patients following blunt injury. <i>The journal of trauma and acute care surgery</i> 81(5): 897-904	- Study design - not diagnostic accuracy or test and treat
Gamal, G.H. (2014) Evaluation of spinal trauma by multi detector computed tomography and magnetic resonance imaging. <i>Egyptian Journal of Radiology and Nuclear Medicine</i> 45(4): 1209-1214	- Not specifically cervical spine injury
Garton, H. J. and Hammer, M. R. (2008) Detection of pediatric cervical spine injury. <i>Neurosurgery</i> 62(3): 700-8; discussion 700	- Study design - only included those with injury already confirmed either on test or reference standard
Gerrelts BD, Petersen EU, Mabry J et al. (1991) Delayed diagnosis of cervical spine injuries. <i>The Journal of trauma</i> 31(12): 1622-1626	- Study design - only included those with injury already confirmed either on test or reference standard
Ghasemi, A.; Haddadi, K.; Shad, A.A. (2015) Comparison of diagnostic accuracy of MRI with and without contrast in diagnosis of traumatic spinal cord injuries. <i>Medicine (United States)</i> 94(43): e1942	- Not specifically cervical spine injury - Study design - only included those with injury already confirmed either on test or reference standard
Griffith B, Bolton C, Goyal N et al. (2011) Screening cervical spine CT in a level I trauma center: overutilization?. <i>AJR. American journal of roentgenology</i> 197(2): 463-467	- Diagnostic test not relevant to review protocol
Haas, Brian M; Hahn, Lewis D; Oliva, Isabel (2019) What is the added sensitivity of non-lateral cervical spine radiographs in the	- Study design - not diagnostic accuracy or test and treat

Study	Code [Reason]
evaluation of acute cervical spine trauma?. Emergency radiology 26(2): 133-138	
Hale, Andrew T, Alvarado, Abraham, Bey, Amita K et al. (2017) X-ray vs. CT in identifying significant C-spine injuries in the pediatric population. Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery 33(11): 1977-1983	- Study design - only included those with injury already confirmed either on test or reference standard
Halpern CH, Milby AH, Guo W et al. (2010) Clearance of the cervical spine in clinically unevaluable trauma patients. Spine 35(18): 1721-1728	- Systematic review used as source of primary studies
Hamard, A., Greffier, J., Bastide, S. et al. (2021) Ultra-low-dose CT versus radiographs for minor spine and pelvis trauma: a Bayesian analysis of accuracy. European Radiology 31(4): 2621-2633	- Not specifically cervical spine injury
Harris, T. J., Blackmore, C. C., Mirza, S. K. et al. (2008) Clearing the cervical spine in obtunded patients. Spine (Phila Pa 1976) 33(14): 1547-53	- Study design - all were CT negative to be included
Hashem, R., Evans, C. C., Farrokhyar, F. et al. (2009) Plain radiography does not add any clinically significant advantage to multidetector row computed tomography in diagnosing cervical spine injuries in blunt trauma patients. J Trauma 66(2): 423-8	- Study design - only included those with injury already confirmed either on test or reference standard
Hennessy, D., Widder, S., Zygum, D. et al. (2010) Cervical spine clearance in obtunded blunt trauma patients: a prospective study. J Trauma 68(3): 576-82	- Study design - all were CT negative to be included
Holmes JF and Akkinpalli R (2005) Computed tomography versus plain radiography to screen for cervical spine injury: a meta-analysis. The Journal of trauma 58(5): 902-905	- Systematic review used as source of primary studies
Holmes, J. F., Mirvis, S. E., Panacek, E. A. et al. (2002) Variability in computed tomography and magnetic resonance imaging in patients with cervical spine injuries. J Trauma 53(3): 524-9; discussion 530	- Study design - only included those with injury already confirmed either on test or reference standard
Huang, Raymond, Ryu, Robert C, Kim, Terrence T et al. (2020) Is magnetic resonance imaging becoming the new computed tomography for	- Study design - not diagnostic accuracy or test and treat

Study	Code [Reason]
cervical spine clearance? Trends in magnetic resonance imaging utilization at a Level I trauma center. The journal of trauma and acute care surgery 89(2): 365-370	
Imerci, A., Canbek, U., Bozoglan, M. et al. (2013) An evaluation of the necessity of computed tomography used for the cervical spine assessment of the patients who present with trauma in the pediatric emergency department. Nobel Medicus 9(2): 91-95	- Study not reported in English
Jeong, S.-Y., Jeon, S.-J., Seol, M. et al. (2020) Diagnostic performance of dual-energy computed tomography for detection of acute spinal fractures. Skeletal Radiology 49(10): 1589-1595	- Not specifically cervical spine injury
Kanji, Hussein D, Neitzel, Andrew, Sekhon, Mypinder et al. (2014) Sixty-four-slice computed tomographic scanner to clear traumatic cervical spine injury: systematic review of the literature. Journal of critical care 29(2): 314e9-13	- Systematic review used as source of primary studies
Kanna, Rishi Mugesh, Gaike, Chandrasekar V, Mahesh, Anupama et al. (2016) Multilevel non-contiguous spinal injuries: incidence and patterns based on whole spine MRI. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 25(4): 1163-9	- Study design - not diagnostic accuracy or test and treat
Keller, S, Bieck, K, Karul, M et al. (2015) Lateralized Odontoid in Plain Film Radiography: Sign of Fractures? A Comparison Study with MDCT. RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin 187(9): 801-7	- Insufficient information to calculate diagnostic accuracy measures
Klein, G. R., Vaccaro, A. R., Albert, T. J. et al. (1999) Efficacy of magnetic resonance imaging in the evaluation of posterior cervical spine fractures. Spine (Phila Pa 1976) 24(8): 771-4	- Study design - only included those with injury already confirmed either on test or reference standard
Laham JL, Cotcamp DH, Gibbons PA et al. (1994) Isolated head injuries versus multiple trauma in pediatric patients: do the same indications for cervical spine evaluation apply?. Pediatric neurosurgery 21(4): 221-6; discussion 226	- Study design - not diagnostic accuracy or test and treat

Study	Code [Reason]
Liao, Shiyao, Jung, Matthias K, Hornig, Lukas et al. (2020) Injuries of the upper cervical spine-how can instability be identified?. International orthopaedics 44(7): 1239-1253	- Review article but not a systematic review
Lindholm, Erika B, Malik, Archana, Parikh, Darshan et al. (2019) Single-lateral cervical radiograph in pediatric trauma is equivalent to multiple views. The journal of trauma and acute care surgery 87(4): 813-817	- Study design - only included those with injury already confirmed either on test or reference standard
Liu, Q, Liu, Q, Zhao, J et al. (2015) Early MRI finding in adult spinal cord injury without radiologic abnormalities does not correlate with the neurological outcome: a retrospective study. Spinal cord 53(10): 750-3	- Study design - not diagnostic accuracy or test and treat - Study design - all were CT negative to be included
MacDonald, R. L., Schwartz, M. L., Mirich, D. et al. (1990) Diagnosis of cervical spine injury in motor vehicle crash victims: how many X-rays are enough?. J Trauma 30(4): 392-7	- X-ray not currently used as initial imaging test in severely injured population
Makino, Yohsuke, Yokota, Hajime, Nakatani, Eiji et al. (2017) Differences between postmortem CT and autopsy in death investigation of cervical spine injuries. Forensic science international 281: 44-51	- Study design - only included those with injury already confirmed either on test or reference standard
Malhotra, A. and Malhotra, A.K. (2019) Evaluation of Cervical Spine Injuries. Current Trauma Reports 5(1): 48-53	- Review article but not a systematic review
Malhotra, Ajay, Wu, Xiao, Kalra, Vivek B et al. (2017) Utility of MRI for cervical spine clearance after blunt traumatic injury: a meta-analysis. European radiology 27(3): 1148-1160	- Study design - all were CT negative to be included
Martin, Matthew J, Bush, Lisa D, Inaba, Kenji et al. (2017) Cervical spine evaluation and clearance in the intoxicated patient: A prospective Western Trauma Association Multi-Institutional Trial and Survey. The journal of trauma and acute care surgery 83(6): 1032-1040	- Secondary publication of an included study that does not provide any additional relevant information
Mavros, Michael N, Kaafarani, Haytham M A, Mejaddam, Ali Y et al. (2015) Additional Imaging in Alert Trauma Patients with Cervical Spine Tenderness and a Negative Computed	- Study design - not diagnostic accuracy or test and treat

Study	Code [Reason]
Tomographic Scan: Is it Needed?. World journal of surgery 39(11): 2685-90	- Study design - all were CT negative to be included
McCallum, J., McLaughlin, P., Hameed, M. et al. (2018) 64-Slice CT compared to MRI to clear cervical spine injury in high-risk GCS score < 14 blunt trauma patients admitted to the ICU. Trauma (United Kingdom) 20(1): 38-45	- Study design - not diagnostic accuracy or test and treat - Study design - all were CT negative to be included
McCutcheon, Lucy, Schmocker, Nicole, Blanksby, Kayla et al. (2015) Best Practice in Diagnostic Imaging after Blunt Force Trauma Injury to the Cervical Spine: A Systematic Review. Journal of medical imaging and radiation sciences 46(2): 231-240	- Systematic review used as source of primary studies
Meinig, H., Doffert, J., Linz, N. et al. (2014) Sensitivity and specificity of ultrasound in spinal trauma in 29 consecutive patients. European Spine Journal	- Diagnostic test not relevant to review protocol
Menaker, J., Philp, A., Boswell, S. et al. (2008) Computed tomography alone for cervical spine clearance in the unreliable patient--are we there yet?. J Trauma 64(4): 898-903; discussion 903	- Study design - all were CT negative to be included
Menaker, J., Stein, D. M., Philp, A. S. et al. (2010) 40-slice multidetector CT: is MRI still necessary for cervical spine clearance after blunt trauma?. Am Surg 76(2): 157-63	- Study design - all were CT negative to be included
Merza, Fadia Abdul-Ameer and Lafta, Ghazwan Alwan (2022) The role of computed tomography and Glasgow Coma Scale in detecting spinal injury associated with traumatic brain injuries. Medicine and pharmacy reports 95(2): 158-164	- Reference standard test not relevant to protocol
Moeri, Michael, Rothenfluh, Dominique A, Laux, Christoph J et al. (2020) Cervical spine clearance after blunt trauma: current state of the art. EFORT open reviews 5(4): 253-259	- Review article but not a systematic review
Mohamed, Mohamed A, Majeske, Karl D, Sachwani-Daswani, Gul et al. (2016) Impact of MRI on changing management of the cervical spine in blunt trauma patients with a 'negative' CT scan. Trauma surgery & acute care open 1(1): e000016	- Study design - not diagnostic accuracy or test and treat - Study design - all were CT negative to be included

Study	Code [Reason]
<p>Moore, Justin M, Hall, Jonathan, Ditchfield, Michael et al. (2017) Utility of plain radiographs and MRI in cervical spine clearance in symptomatic non-obtunded pediatric patients without high-impact trauma. <i>Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery</i> 33(2): 249-258</p>	<p>- Population not relevant to this review protocol</p>
<p>Morais, D.F., De Melo Neto, J.S., Meguins, L.C. et al. (2014) Clinical applicability of magnetic resonance imaging in acute spinal cord trauma. <i>European Spine Journal</i> 23(7): 1457-1463</p>	<p>- Study design - not diagnostic accuracy or test and treat</p> <p>- Not specifically cervical spine injury</p>
<p>Mower, W. R., Hoffman, J. R., Pollack, C. V., Jr. et al. (2001) Use of plain radiography to screen for cervical spine injuries. <i>Ann Emerg Med</i> 38(1): 1-7</p>	<p>- Study design - only included those with injury already confirmed either on test or reference standard</p>
<p>Murphy, Joshua M; Park, Paul; Patel, Rakesh D (2014) Cost-effectiveness of MRI to assess for posttraumatic ligamentous cervical spine injury. <i>Orthopedics</i> 37(2): e148-52</p>	<p>- Study design - not diagnostic accuracy or test and treat</p>
<p>Nazir, Muhammad, Khan, Shahbaz Ali, Raja, Riaz A et al. (2012) Cervical spinal injuries in moderate to severe head injuries. <i>Journal of Ayub Medical College, Abbottabad : JAMC</i> 24(34): 100-2</p>	<p>- Study design - not diagnostic accuracy or test and treat</p>
<p>Nigrovic, L. E., Rogers, A. J., Adalgais, K. M. et al. (2012) Utility of plain radiographs in detecting traumatic injuries of the cervical spine in children. <i>Pediatr Emerg Care</i> 28(5): 426-32</p>	<p>- Study design - only included those with injury already confirmed either on test or reference standard</p>
<p>Nunn, C., Negus, S., Lawrence, T. et al. (2020) Have changes in computerised tomography guidance positively impacted detection of cervical spine injury in children? A review of the Trauma Audit and Research Network data. <i>Trauma (United Kingdom)</i></p>	<p>- Study design - not diagnostic accuracy or test and treat</p>
<p>Nuñez DB, Zuluaga A, Fuentes-Bernardo DA et al. (1996) Cervical spine trauma: how much more do we learn by routinely using helical CT?. <i>Radiographics : a review publication of the Radiological Society of North America, Inc</i> 16(6): 1307</p>	<p>- Study design - only included those with injury already confirmed either on test or reference standard</p>

Study	Code [Reason]
O'Boynick, C.P.; Lonergan, T.M.; Place, H.M. (2015) Clearing the C-spine in obtunded trauma patients based on admission CT: A prospective randomized trial. <i>Spine</i> 2015(supplement2): 416	- Full text paper not available
Oh, Jason Jaeseong; Asha, Stephen Edward; Curtis, Kate (2016) Diagnostic accuracy of flexion-extension radiography for the detection of ligamentous cervical spine injury following a normal cervical spine computed tomography. <i>Emergency medicine Australasia</i> : EMA 28(4): 450-5	- Study design - all were CT negative to be included
Ojaghiahghi, S., Vahdati, S.S., Tarzamani, M.K. et al. (2019) Diagnostic value of bedside ultrasound for detecting cervical spine injuries in patients with severe multiple trauma. <i>Trauma Monthly</i> 24(5): e85199	- Diagnostic test not relevant to review protocol
Onoue, Keita, Farris, Chad, Burley, Hannah et al. (2019) Role of cervical spine MRI in the setting of negative cervical spine CT in blunt trauma: Critical additional information in the setting of clinical findings suggestive of occult injury. <i>Journal of neuroradiology = Journal de neuroradiologie</i>	- Study design - not diagnostic accuracy or test and treat - Study design - all were CT negative to be included
Overmann, Kevin M; Robinson, Bryce R H; Eckman, Mark H (2020) Cervical spine evaluation in pediatric trauma: A cost-effectiveness analysis. <i>The American journal of emergency medicine</i> 38(11): 2347-2355	- Study design - not diagnostic accuracy or test and treat
Padayachee, L., Cooper, D. J., Irons, S. et al. (2006) Cervical spine clearance in unconscious traumatic brain injury patients: dynamic flexion-extension fluoroscopy versus computed tomography with three-dimensional reconstruction. <i>J Trauma</i> 60(2): 341-5	- Study design - all were CT negative to be included
Panczykowski, D. M.; Tomycz, N. D.; Okonkwo, D. O. (2011) Comparative effectiveness of using computed tomography alone to exclude cervical spine injuries in obtunded or intubated patients: meta-analysis of 14,327 patients with blunt trauma. <i>J Neurosurg</i> 115(3): 541-9	- Systematic review used as source of primary studies
Patel, M S, Grannum, S, Tariq, A et al. (2013) Are soft tissue measurements on lateral cervical spine X-rays reliable in the assessment of traumatic injuries?. <i>European journal of trauma</i>	- Full text paper not available

Study	Code [Reason]
and emergency surgery : official publication of the European Trauma Society 39(6): 613-8	
Patel, Mayur B, Humble, Stephen S, Cullinane, Daniel C et al. (2015) Cervical spine collar clearance in the obtunded adult blunt trauma patient: a systematic review and practice management guideline from the Eastern Association for the Surgery of Trauma. The journal of trauma and acute care surgery 78(2): 430-41	- Systematic review used as source of primary studies
Plackett, Timothy P, Wright, Franklin, Baldea, Anthony J et al. (2016) Cervical spine clearance when unable to be cleared clinically: a pooled analysis of combined computed tomography and magnetic resonance imaging. American journal of surgery 211(1): 115-21	- Systematic review used as source of primary studies - Study design - all were CT negative to be included
Platzer, P., Jaendl, M., Thalhammer, G. et al. (2006) Clearing the cervical spine in critically injured patients: a comprehensive C-spine protocol to avoid unnecessary delays in diagnosis. Eur Spine J 15(12): 1801-10	- Study design - only included those with injury already confirmed either on test or reference standard
Plumb, J. O. and Morris, C. G. (2012) Clinical review: Spinal imaging for the adult obtunded blunt trauma patient: update from 2004. Intensive Care Med 38(5): 752-71	- Systematic review used as source of primary studies
Raja, R.; Arooj, S.; Mahmood, H. (2018) Role of magnetic resonance imaging in acute spinal cord trauma. Pakistan Journal of Medical and Health Sciences 12(3): 925-929	- Study design - not diagnostic accuracy or test and treat
Russin, Jonathan J, Attenello, Frank J, Amar, Arun P et al. (2013) Computed tomography for clearance of cervical spine injury in the unevaluable patient. World neurosurgery 80(34): 405-13	- Systematic review used as source of primary studies
Sanchez, B., Waxman, K., Jones, T. et al. (2005) Cervical spine clearance in blunt trauma: evaluation of a computed tomography-based protocol. J Trauma 59(1): 179-83	- Diagnostic test not relevant to review protocol
Sarani, B., Waring, S., Sonnad, S. et al. (2007) Magnetic resonance imaging is a useful adjunct in the evaluation of the cervical spine of injured patients. J Trauma 63(3): 637-40	- Full text paper not available

Study	Code [Reason]
Satahoo, Shevonne S, Davis, James S, Garcia, George D et al. (2014) Sticking our neck out: is magnetic resonance imaging needed to clear an obtunded patient's cervical spine?. The Journal of surgical research 187(1): 225-9	<ul style="list-style-type: none"> - Study design - not diagnostic accuracy or test and treat - Study design - all were CT negative to be included
Savakus, Jonathan C, Weinberg, Douglas S, Moore, Timothy A et al. (2020) Prevertebral Soft-Tissue Swelling at C7 Is Highly Sensitive for Cervical Spine Ligamentous Injury Study Type: Retrospective Cohort Study. Journal of the American Academy of Orthopaedic Surgeons. Global research & reviews 4(4)	<ul style="list-style-type: none"> - Diagnostic test not relevant to review protocol
Schenarts PJ, Diaz J, Kaiser C et al. (2001) Prospective comparison of admission computed tomographic scan and plain films of the upper cervical spine in trauma patients with altered mental status. The Journal of trauma 51(4): 663	<ul style="list-style-type: none"> - Study design - only included those with injury already confirmed either on test or reference standard
Schoenwaelder, M.; Maclaurin, W.; Varma, D. (2009) Assessing potential spinal injury in the intubated multitrauma patient: does MRI add value?. Emerg Radiol 16(2): 129-32	<ul style="list-style-type: none"> - Study design - all were CT negative to be included
Schoneberg, C, Schweiger, B, Hussmann, B et al. (2013) Diagnosis of cervical spine injuries in children: a systematic review. European journal of trauma and emergency surgery : official publication of the European Trauma Society 39(6): 653-65	<ul style="list-style-type: none"> - Systematic review used as source of primary studies
Schuster, R., Waxman, K., Sanchez, B. et al. (2005) Magnetic resonance imaging is not needed to clear cervical spines in blunt trauma patients with normal computed tomographic results and no motor deficits. Arch Surg 140(8): 762-6	<ul style="list-style-type: none"> - Diagnostic test not relevant to review protocol
Shyu, J.Y., Khurana, B., Soto, J.A. et al. (2020) ACR Appropriateness Criteria Major Blunt Trauma. Journal of the American College of Radiology 17(5supplement): 160-s174	<ul style="list-style-type: none"> - Review article but not a systematic review
Sierink, J C, van Lieshout, W A M, Beenen, L F M et al. (2013) Systematic review of flexion/extension radiography of the cervical spine in trauma patients. European journal of radiology 82(6): 974-81	<ul style="list-style-type: none"> - Systematic review used as source of primary studies

Study	Code [Reason]
Singh, S., Garg, R., Singh, P. et al. (2015) Diagnosing Cervical Spine Injury in Severe Head Injury: A Case for Replacing Plain Radiography With Computed Tomographic Scan of the Cervical Spine. Indian Journal of Neurotrauma 12(1): 35-40	- Reference standard test not relevant to protocol
Smith, Jackie S (2014) A synthesis of research examining timely removal of cervical collars in the obtunded trauma patient with negative computed tomography: an evidence-based review. Journal of trauma nursing : the official journal of the Society of Trauma Nurses 21(2): 63-7	- Study design - all were CT negative to be included
Soult, M. C., Weireter, L. J., Britt, R. C. et al. (2012) MRI as an adjunct to cervical spine clearance: a utility analysis. Am Surg 78(7): 741-4	- Study design - all were CT negative to be included
Stassen, N. A., Williams, V. A., Gestring, M. L. et al. (2006) Magnetic resonance imaging in combination with helical computed tomography provides a safe and efficient method of cervical spine clearance in the obtunded trauma patient. J Trauma 60(1): 171-7	- Study design - excluded those positive on initial imaging (X-ray)
Sutherland, M., Bourne, M., McKenney, M. et al. (2021) Utilization of computerized tomography and magnetic resonance imaging for diagnosis of traumatic C-Spine injuries at a level 1 trauma center: A retrospective Cohort analysis. Annals of Medicine & Surgery 68: 102566	- Reference standard test not relevant to protocol (MRI, and was not able to calculate MRI+CT as reference standard)
Tomycz, N. D., Chew, B. G., Chang, Y. F. et al. (2008) MRI is unnecessary to clear the cervical spine in obtunded/comatose trauma patients: the four-year experience of a level I trauma center. J Trauma 64(5): 1258-63	- Study design - all were CT negative to be included
Veiga, Joana Raquel Santos and Mitchell, Kay (2019) Cervical spine clearance in the adult obtunded blunt trauma patient: A systematic review. Intensive & critical care nursing 51: 57-63	- Systematic review used as source of primary studies
Wu, Xiao, Malhotra, Ajay, Geng, Bertie et al. (2018) Cost-effectiveness of Magnetic Resonance Imaging in Cervical Clearance of Obtunded Blunt Trauma After a Normal Computed Tomographic Finding. JAMA surgery 153(7): 625-632	- Study design - not diagnostic accuracy or test and treat

Study	Code [Reason]
Wu, Xiao, Malhotra, Ajay, Geng, Bertie et al. (2018) Cost-effectiveness of Magnetic Resonance Imaging in Cervical Spine Clearance of Neurologically Intact Patients With Blunt Trauma. <i>Annals of emergency medicine</i> 71(1): 64-73	- Study design - not diagnostic accuracy or test and treat
Yasin, A.; Saeed, U.; Munir, M. (2017) Magnetic Resonance Imaging (MRI) diagnostic accuracy in acute spinal column injuries. <i>Pakistan Journal of Medical and Health Sciences</i> 11(3): 971-972	- Not specifically cervical spine injury
Zhuge, W., Ben-Galim, P., Hipp, J.A. et al. (2015) Efficacy of MRI for Assessment of Spinal Trauma. <i>Journal of Spinal Disorders and Techniques</i> 28(4): 147-151	- Not specifically cervical spine injury

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2006 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.