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Diagnostic management strategies for adults and children with minor head injury: a systematic review and an economic evaluation

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Appendix 1

Diagnostic accuracy and management strategies for minor head injury review: literature search strategies – a MEDLINE example

Database searched: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)

Platform or provider used: OvidSP

Date of coverage: 1950 to March 2010

Search undertaken: initial search 20 April 2009

Updated search: 11 March 2010

1. *Craniocerebral Trauma/
2. head injur$.tw.
3. 1 or 2
4. prognosis.sh.
5. diagnosed.tw.
6. cohort:.mp.
7. predictor:.tw.
8. death.tw.
9. exp models, statistical/
10. (clinical assess* or decision rule* or prediction rule*).tw.
11. 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp "Sensitivity and Specificity"/
13. sensitivity.tw.
14. specificity.tw.
15. ((pre-test or pretest) adj probability).tw.
16. post-test probability.tw.
17. predictive value$.tw.
18. likelihood ratio$.tw.
19. 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 3 and (11 or 19)

Appendix 2

The modified QUADAS tool for the methodological assessment of diagnostic studies

	QUADAS[a] criterion	Criteria met	Criteria defined
1	Was the spectrum of patients representative of the patients who will receive the test in practice?	Yes	Unselected, prospective patients (children or adults) with early head injury (GCS 13–15, within 48 hours of presentation)
		No	All other patient spectra including retrospectively selected patient spectra, and spectra including only those who had CT
		Unclear	If insufficient details were provided to make a judgement as to whether the patient spectrum would be scored as 'yes'
2	Were selection criteria clearly described?	Yes	Enough details are provided of how patients were selected so that the selection process could be replicated
		No	Insufficient details are presented
		Unclear	NA
3a	*Criteria modified* Is the reference standard likely to correctly classify ICI? (Where ICI is not an outcome, this item may be classed as not applicable)	Yes	ICI: All of cohort have CT or MRI within 24 hours of admission
		No	All other reference standards
		Unclear	If details of the reference standard are not reported
3b	*Criteria modified* Is the reference standard likely to correctly classify need for neurosurgery? (Where need for neurosurgery is not an outcome, this item may be classed as not applicable)	Yes	Neurosurgery: all of the cohort have follow-up 30 days or more after the injury
		No	All other reference standards
		Unclear	If details of the reference standard are not reported
4	*Not used: not relevant to this review*[b] Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	Yes	
		No	
		Unclear	
5a	*Criteria modified* Partial verification bias. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis for ICI?	Yes	If the whole sample or random selection of the sample received a reference standard
		No	If only a selected sample received a reference standard
		Unclear	If it was not clear whether or not all the patients received a reference standard
5b	*Criteria modified* Partial verification bias. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis for neurosurgery?	Yes	If the whole sample or random selection of the sample received a reference standard
		No	If only a selected sample received a reference standard
		Unclear	If it was not clear whether or not all the patients received a reference standard
6a	*Criteria modified* Differential verification bias. Did all patients receive the same reference standard for ICI regardless of the index test result?	Yes	If patients received a reference standard regardless of the index test result
		No	If patients received a reference standard based on part or all of the index test result
		Unclear	If it was not clear whether or not the index test result influenced which reference standard was used, including where physician discretion may incorporate part or all of the index test

continued

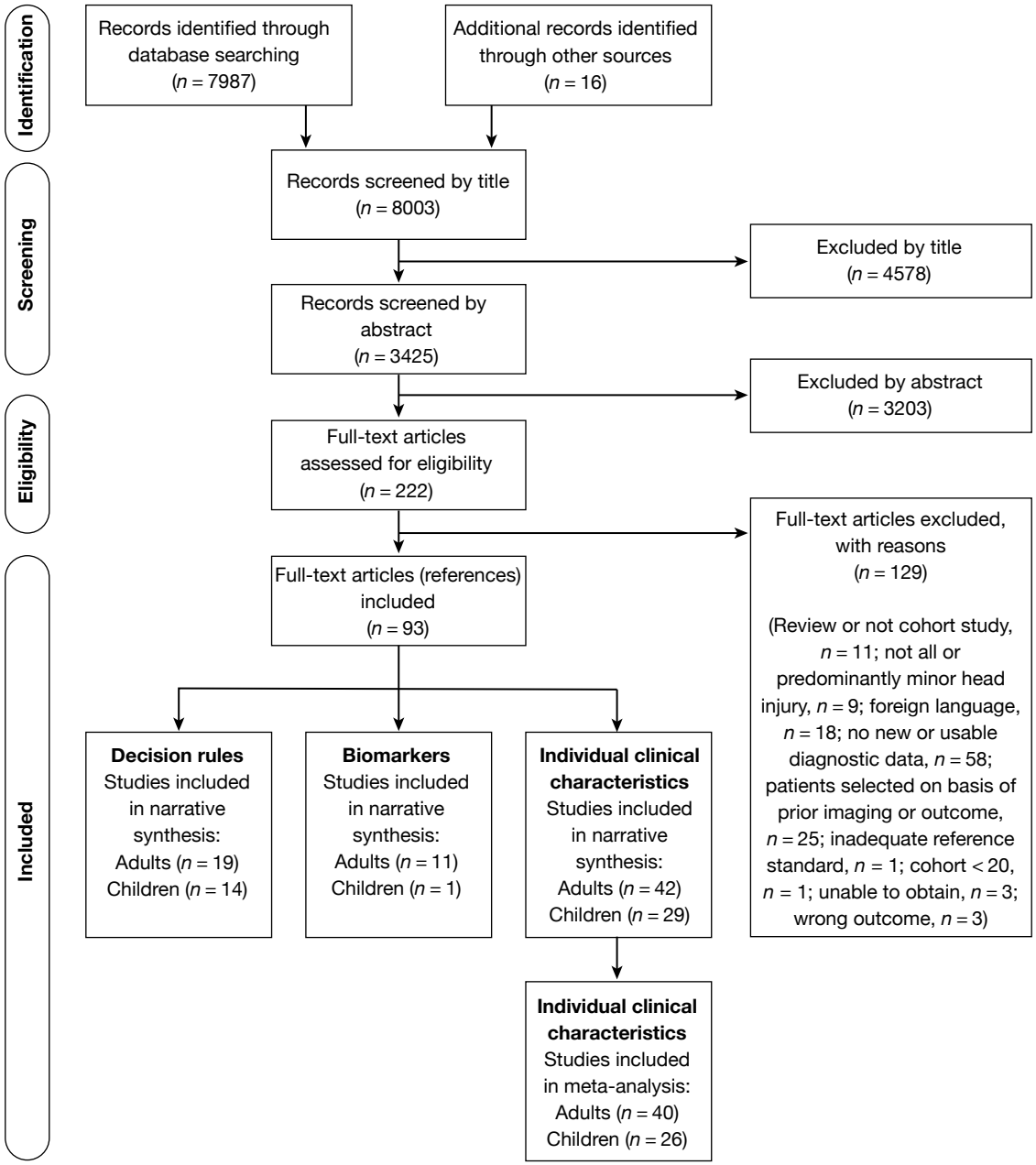
	QUADAS[a] criterion	Criteria met	Criteria defined
6b	*Criteria modified* Differential verification bias. Did all patients receive the same reference standard for neurosurgery regardless of the index test result?	Yes	If patients received a reference standard regardless of the index test result
		No	If patients received a reference standard based on part or all of the index test result
		Unclear	If it was not clear whether the index test result influenced which reference standard was used, including where physician discretion may incorporate part or all of the index test
7	*Not used: not relevant to this review*[c] Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	Yes	
		No	
		Unclear	
8	Was the execution of the index test described in sufficient detail to permit replication of the test?	Yes	If sufficient details of test standard execution were reported so that the test/reference standard could reasonably be replicated
		No	If sufficient details are not reported
		Unclear	NA
9	Was the execution of the reference standard described in sufficient detail to permit its replication?	Yes	If sufficient details of reference standard execution were reported so that the test/reference standard could reasonably be replicated
		No	If sufficient details are not reported
		Unclear	NA
10	Test review bias. Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	If the index test was interpreted without knowledge (blinding) of the results of the reference standard and vice versa
			If one test was clearly interpreted before the results of the other test were available then this should be scored as 'yes'
		No	If the person interpreting the index test was aware of the results of the reference standard or vice versa
		Unclear	If no information is provided regarding whether tests were interpreted blindly
11	Diagnostic review bias. Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	If the index test was interpreted without knowledge (blinding) of the results of the reference standard and vice versa
			If one test was clearly interpreted before the results of the other test were available then this should be scored as 'yes'
		No	If the person interpreting the index test was aware of the results of the reference standard or vice versa
		Unclear	If no information is provided regarding whether tests were interpreted blindly
12	Clinical review bias. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	Yes	If the article states the following information was available: description of symptoms, site of injury, patient characteristics, e.g. clinician may be blinded to data that are normally available to them
		No	If not as above
		Unclear	If details on the availability of clinical data were not reported
13	Were uninterpretable/intermediate test results reported?	Yes	If details are provided on uninterpretable/intermediate test results
		No	If there appear to be some on uninterpretable/intermediate but the results of those are not reported
		Unclear	If it is not clear whether there were any uninterpretable/ intermediate test results

	QUADAS[a] criterion	Criteria met	Criteria defined
14	Were withdrawals from the study explained?	Yes	If all patients who entered into the study were accounted for
		No	If it appears that some of the participants who entered the study did not complete the study, i.e. did not receive both the index test and reference standard, and these patients were not accounted for
		Unclear	If it is not clear whether all patients who entered the study were accounted for

NA, not applicable.
a The QUADAS tool used was Whiting *et al.*[47]
b Disease progression bias was not relevant because the time element was addressed by criteria 3a and 3b.
c Incorporation bias was not relevant because the reference standard was always independent of the index test.

Appendix 3

Diagnostic accuracy review – PRISMA (adapted) flow chart



Appendix 4

Diagnostic accuracy review – table of excluded studies with rationale

Author, year	Reason for exclusion
Adams *et al.* 2001[192]	No useable diagnostic data
Andronikou *et al.* 2003[193]	No useable diagnostic data
Anglin *et al.* 1998[194]	Not all or predominantly MHI: gunshot wounds
Anonymous 1994[195]	No useable diagnostic data
Anonymous 2007[196]	Review
Ariel *et al.* 2006[197]	Foreign language
Atif and Qureshi 2001[198]	Wrong outcome – predicting skull fracture
Baglaj *et al.* 2005[199]	Unable to obtain
Balla and Elstein 1984[200]	Review
Bamvita *et al.* 2006[201]	Foreign language
Bazarian *et al.* 2006[202]	No useable diagnostic data
Beaudin *et al.* 2007[203]	No useable diagnostic data
Benito Fernández *et al.* 1998[204]	No useable diagnostic data
Berger *et al.* 2002[205]	Not cohort study (case control); no useable diagnostic data
Bernard *et al.* 1983[206]	Foreign language
Biberthaler *et al.* 2001[207]	No useable diagnostic data
Biberthaler *et al.* 2004[208]	Foreign language
Block 2001[209]	Review
Boran *et al.* 2005[210]	Foreign language
Bouvier *et al.* 2009[211]	Foreign language
Brown *et al.* 1994[152]	No useable diagnostic data
Browning *et al.* 2005[154]	No useable diagnostic data
Chan *et al.* 1990[212]	Patients selected on the basis of outcome
Chan *et al.* 2005[213]	No useable diagnostic data
Clement 2006[214]	No new data
Cummins 1992[215]	Review
Dahl-Grove *et al.* 1995[216]	Patients selected on the basis of outcome: negative CT scan
de Andrade *et al.* 2006[217]	No useable diagnostic data
de Boussard *et al.* 2005[218]	Wrong outcome – symptoms and signs of cognitive impairment
de Boussard *et al.* 2006[219]	Not cohort study
Dunning *et al.* 2004[220]	No useable diagnostic data
Duus *et al.* 1993[221]	No useable diagnostic data
Edna 1983[222]	Patients selected on the basis of outcome
Edna 1983[223]	Patients selected on the basis of outcome
Edna and Cappelen 1984[224]	Patients selected on the basis of outcome
Espersen and Petersen 1982[225]	No useable diagnostic data
Fabbri *et al.* 2004[226]	No new data
Fabbri *et al.* 2004[153]	No useable diagnostic data
Fong *et al.* 2008[155]	No useable diagnostic data
Af Geijerstam *et al.* 2006[37]	Wrong outcome – GOS

continued

Author, year	Reason for exclusion
Geyer *et al.* 2009[227]	No useable diagnostic data
Gonzalez *et al.* 2007[228]	Foreign language
Gorelick *et al.* 2008[229]	No useable diagnostic data
Greenes and Schutzman 1998[230]	Patients selected on the basis of outcome
Gruskin *et al.* 1999[231]	Patients selected on the basis of outcome
Gupta *et al.* 2005[232]	No useable diagnostic data
Gutman *et al.* 1992[233]	No useable diagnostic data
Harris *et al.* 2008[234]	No useable diagnostic data
Hassan *et al.* 2005[22]	No useable diagnostic data
Hoffmann *et al.* 2001[235]	Not all or predominantly MHI: includes spontaneous injury
Hollingworth *et al.* 2007[236]	Not all or predominantly MHI: progressive injury
Holsti *et al.* 2005[237]	Patients selected on the basis of outcome
Benito Fernández 1998[238]	Foreign language
Jones *et al.* 2008[239]	No useable diagnostic data
Kahraman *et al.* 2006[240]	Patients selected on the basis of outcome
Kakarieka *et al.* 1994[241]	Patients selected on the basis of outcome
Kavalci *et al.* 2007[242]	No useable diagnostic data
Kelly *et al.* 1988[33]	Patients selected on the basis of outcome
Kerr *et al.* 2005[156]	No useable diagnostic data
King and Haddock 2009[243]	No useable diagnostic data
Knuckey *et al.* 1989[244]	Patients selected on the basis of outcome
Kuhne *et al.* 2003[245]	Foreign language
Kuppermann *et al.* 2007[246]	No useable diagnostic data. Protocol only, full study being prepared for publication
Lehmann *et al.* 1997[247]	Foreign language
Levi *et al.* 1991[248]	No useable diagnostic data
Livingston *et al.* 1991[249]	No useable diagnostic data
Lloyd *et al.* 1997[250]	Not all or predominantly MHI (assumed)
Loroni *et al.* 1996[157]	No useable diagnostic data
Lucchi *et al.* 1995[251]	Foreign language
Mahmood 2000[252]	Unable to obtain
Mandera *et al.* 1999[253]	Patients selected on the basis of outcome
Markle *et al.* 1992[254]	No useable diagnostic data
Marshall *et al.* 1998[255]	No useable diagnostic data
Marti-Fabregas *et al.* 2003[256]	Patients selected on the basis of outcome
Martinot *et al.* 2008[257]	Foreign language
Massaro *et al.* 1996[258]	Patients selected on the basis of outcome
Masters 1980[259]	Inadequate reference standard
Matsumoto *et al.* 1988[260]	Foreign language
Mattox *et al.* 1989[261]	No useable diagnostic data
Meier 1983[262]	Review
Memon *et al.* 1995[263]	No useable diagnostic data
Mendelow *et al.* 2003[264]	Review
Mendelow *et al.* 2008[265]	Review
Menon and Harrison 2008[266]	Review
Meyer *et al.* 2006[267]	Foreign language
Mikhail *et al.* 1992[268]	No useable diagnostic data
Miller *et al.* 1990[269]	Patients selected on the basis of outcome
Mohanty *et al.* 1991[270]	No useable diagnostic data
Murgio *et al.* 2003[271]	Unable to obtain
Mussack *et al.* 2000[272]	No useable diagnostic data

Author, year	Reason for exclusion
Muszynski *et al.* 1999[273]	Patients selected on the basis of outcome
Muthukumar *et al.* 1993[274]	Not all or predominantly MHI
Naeimi *et al.* 2006[275]	Not all or predominantly MHI
Nagy *et al.* 1999[276]	No useable diagnostic data
Oertel *et al.* 2002[277]	Not all or predominantly MHI: progressive injury
Oh *et al.* 2007[278]	Not all or predominantly MHI: includes chronic injury
Orrison *et al.* 1994[279]	No useable diagnostic data
Ortiz *et al.* 2006[280]	Foreign language
Ortiz and Paneque 2006[281]	Foreign language
Owings *et al.* 1998[282]	No useable diagnostic data
Palchak *et al.* 2009[283]	No new data
Pasman *et al.* 1995[284]	No useable diagnostic data
Pretto *et al.* 2000[285]	No useable diagnostic data
Rathlev *et al.* 2006[286]	No new data
Reinus *et al.* 1994[287]	Not all or predominantly MHI: includes chronic or spontaneous head injury
Richless *et al.* 1993[28]	No useable diagnostic data
Rivas *et al.* 1988[288]	Patients selected on the basis of outcome
Sainsbury and Sibert 1984[289]	Patients selected on the basis of outcome
Sanus *et al.* 2004[290]	Patients selected on the basis of outcome
Savastio *et al.* 1991[291]	Foreign language
Schultke *et al.* 2009[189]	No useable diagnostic data
Servadei *et al.* 1989[292]	Patients selected on the basis of outcome
Shane and Fuchs 1997[293]	Patients selected on the basis of prior imaging or outcome
Shravat *et al.* 2006[158]	No useable diagnostic data
Sifri *et al.* 2006[294]	Patients selected on the basis of prior imaging or outcome
Smits *et al.* 2007[295]	No new data
Stein *et al.* 1993[296]	No useable diagnostic data
Sultan *et al.* 2004[21]	No useable diagnostic data
Taheri *et al.* 1993[297]	No useable diagnostic data
Teasdale *et al.* 1990[298]	No useable diagnostic data
Thompson *et al.* 2005[159]	No useable diagnostic data
Turedi *et al.* 2008[299]	Not cohort study (patients selected on basis of age)
Velmahos *et al.* 2006[300]	Patients selected on the basis of outcome
Vogelbaum *et al.* 1998[301]	No useable diagnostic data
Voss *et al.* 1995[302]	No useable diagnostic data
Willis *et al.* 2008[303]	No useable diagnostic data
Yamamoto and Ogata 1981[304]	Foreign language
Yanagawa *et al.* 2000[305]	Patients selected on the basis of outcome (survived for 1 week)
Zimmerman *et al.* 1986[306]	Cohort of <20

Appendix 5

Individual clinical characteristics in adults – data for meta-analysis

Intracranial injury in adults

Intoxication (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	264	18.8	87.9	18.5	9.8 to 30.2	87.8	83.4 to 91.4	0.930	0.797 to 1.033	1.51	0.79 to 2.64
Borczuk 1995[55]	1448	25.2	68.5	26.4	19.5 to 34.3	68.8	66.3 to 71.2	1.070	0.950 to 1.180	0.85	0.62 to 1.11
Haydel 2000[27]	520	61.1	67.4	51.6	36.2 to 67.2	67.3	63.1 to 71.4	0.720	0.486 to 0.953	1.58	1.09 to 2.12
Stiell 2001[26]	3121	18.1	88.2	18.0	13.9 to 22.8	88.2	87.0 to 89.4	0.929	0.875 to 0.977	1.53	1.17 to 1.97
Mack 2003[110]	133	15.8	94.7	13.6	5.5 to 26.9	93.2	88.3 to 96.7	0.929	0.790 to 1.015	1.98	0.83 to 4.71
Ibanez and Arikan 2004[60]	1101	6.0	94.0	8.2	3.9 to 14.4	94.0	92.4 to 95.3	0.977	0.911 to 1.026	1.36	0.63 to 2.46
Fabbri 2005[57]	7955	26.9	91.6	26.2	22.6 to 30.0	91.6	90.9 to 92.2	0.806	0.764 to 0.846	3.10	2.63 to 3.63
Mower 2005[62]	13,728	19.0	75.6	19.3	16.8 to 21.9	75.7	74.9 to 76.4	1.067	1.031 to 1.101	0.79	0.69 to 0.90
Stiell 2005[46]	1822	13.4	84.4	15.4	9.6 to 22.4	84.5	82.8 to 86.2	1.002	0.918 to 1.074	0.99	0.61 to 1.46
Ono 2007[63]	1064	36.0	72.7	34.1	23.5 to 46.5	72.8	70.0 to 75.5	0.905	0.736 to 1.055	1.25	0.86 to 1.7
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	10	<0.001	<0.001	21.4	13.5 to 31.4	84.6	76.7 to 90.3	0.931	0.844 to 1.007	1.38	0.97 to 1.99

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Fall – any (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	302	16.4	81.4	19.3	12.7 to 26.3	81.6	77.1 to 85.6	0.990	0.921 to 1.060	1.05	0.74 to 1.4
Jeret 1993[107]	712	6.0	90.9	8.6	4.3 to 14.7	90.7	88.3 to 92.7	1.008	0.943 to 1.058	0.92	0.47 to 1.59
Schynoll 1993[118]	264	56.3	44.8	61.3	49.7 to 72.6	47.0	40.8 to 53.1	0.822	0.597 to 1.077	1.16	0.94 to 1.4
Cook 1994[100]	107	22.2	71.6	30.7	19.8 to 42.5	72.4	64.1 to 79.8	0.956	0.867 to 1.051	1.12	0.86 to 1.32
Tsai 1994[125]	186	22.5	75.3	26.0	17.9 to 34.4	76.1	70.1 to 81.6	0.971	0.902 to 1.053	1.09	0.83 to 1.3
Borczuk 1995[55]	1448	36.1	70.0	34.5	29.3 to 40.0	69.8	67.5 to 72.2	0.938	0.866 to 1.008	1.14	0.98 to 1.31
Miller 1996[111]	1382	25.0	73.0	29.3	23.0 to 34.6	73.4	71.0 to 75.6	0.964	0.899 to 1.048	1.10	0.87 to 1.3
Stiell 2001[26]	3121	42.1	70.1	36.5	31.9 to 42.3	69.6	67.9 to 71.2	0.914	0.827 to 0.978	1.20	1.05 to 1.40
Mack 2003[110]	133	42.1	58.8	45.1	34.4 to 57.3	60.8	52.6 to 68.3	0.902	0.759 to 1.039	1.16	0.94 to 1.36
Ono 2007[63]	1064	32.0	63.2	40.8	32.8 to 48.0	63.9	61.0 to 66.7	0.927	0.824 to 1.052	1.13	0.91 to 1.31
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	10	<0.001	<0.001	31.3	20.3 to 44.3	72.0	62.2 to 80.2	0.953	0.871 to 1.024	1.12	0.93 to 1.29

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Fall from a height (intracranial injury – adults)

	Observed estimates		Fixed effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ono 2007[63]	28.0	87.8	28.0	17.3 to 41.9	87.8	85.6 to 89.6	0.820	0.689 to 0.977	2.29	1.43 to 3.68

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Dizziness (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Cook 1994[100]	107	12.5	73.2	18.7	11.7 to 27.3	73.7	69.4 to 78.1	1.103	0.969 to 1.227	0.71	0.43 to 1.10
Mack 2003[110]	133	10.5	79.8	18.9	11.8 to 27.6	74.3	70.5 to 80.2	1.091	0.946 to 1.208	0.74	0.45 to 1.19
Ibanez and Arikan 2004[60]	1101	21.7	72.7	18.6	12.1 to 26.8	73.3	70.7 to 75.8	1.109	0.995 to 1.210	0.70	0.45 to 1.02
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.482	0.267	18.7	11.9 to 27.3	73.8	70.2 to 78.1	1.101	0.970 to 1.217	0.72	0.44 to 1.09

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Coagulopathy (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Borczuk 1995[55]	1448	6.7	96.8	7.2	4.0 to 11.7	96.9	95.9 to 96.9	0.958	0.913 to 0.992	2.29	1.22 to 3.88
Arienta 1997[54]	10,000	0.6	100.0	0.2	0.0 to 1.3	100.0	99.9 to 100.0	0.998	0.988 to 1.000	5.41	0.42 to 40.81
Haydel 2000[27]	520	0.0	99.8	0.7	0.0 to 3.5	99.8	99.2 to 99.8	0.995	0.970 to 1.001	3.53	0.50 to 21.92
Mack 2003[110]	133	15.8	86.8	20.1	8.9 to 36.0	88.4	81.9 to 88.4	0.904	0.734 to 1.044	1.75	0.73 to 3.36
Ibanez and Arikan 2004[60]	1101	32.5	90.3	29.2	20.6 to 39.3	90.2	88.2 to 90.2	0.786	0.673 to 0.882	2.96	2.02 to 4.22
Fabbri 2005[57]	7955	12.4	97.3	11.7	9.2 to 14.6	97.3	96.9 to 97.3	0.908	0.878 to 0.934	4.33	3.28 to 5.62
Mower 2005[62]	13,728	5.0	96.1	5.4	4.1 to 7.1	96.1	95.8 to 96.1	0.984	0.967 to 0.999	1.39	1.03 to 1.85
Saboori 2007[67]	682	0.0	99.8	0.6	0.0 to 2.9	99.9	99.4 to 99.9	0.996	0.974 to 1.001	3.64	0.46 to 23.50
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	8	<0.001	<0.001	4.9	0.6 to 16.0	98.2	93.3 to 99.8	0.968	0.897 to 0.999	3.27	1.21 to 7.52

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Chronic alcohol (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Arienta 1997[54]	10,000	0.6	100.0	0.4	0.0 to 2.1	100.0	99.9 to 100.0	0.996	0.979 to 1.000	9.52	0.95 to 62.07
Stiell 2001[26]	3121	17.3	89.7	14.0	11.2 to 17.4	89.5	88.4 to 90.6	0.961	0.923 to 0.993	1.34	1.06 to 1.68
Ibanez and Arikan 2004[60]	1101	2.4	95.8	7.4	4.2 to 10.8	96.1	94.8 to 97.1	0.964	0.931 to 0.996	1.86	1.11 to 2.82
Stiell 2005[46]	2707	15.2	85.1	16.9	13.3 to 21.0	85.2	83.8 to 86.6	0.975	0.926 to 1.019	1.15	0.89 to 1.4
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	4	<0.001	<0.001	5.9	0.7 to 40.8	97.6	49.5 to 99.8	0.973	0.933 to 1.186	2.00	0.79 to 9.03

a Of posterior distribution for Bayesian meta-analyses..
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Assault (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	302	27.3	83.4	19.4	14.1 to 26.1	81.6	77.1 to 85.8	0.987	0.928 to 1.036	1.06	0.85 to 1.32
Jeret 1993[107]	712	37.3	70.1	10.5	7.6 to 13.9	89.3	88.1 to 90.4	1.002	0.964 to 1.036	0.98	0.71 to 1.31
Schynoll 1993[118]	264	3.1	88.8	9.9	5.4 to 15.4	89.8	85.9 to 93.1	1.003	0.962 to 1.039	0.97	0.64 to 1.35
Cook 1994[100]	107	66.7	37.8	66.8	48.6 to 82.9	39.1	30.1 to 48.4	0.847	0.469 to 1.315	1.10	0.81 to 1.36
Tsai 1994[125]	186	5.0	96.6	3.7	1.3 to 7.9	95.9	92.4 to 98.1	1.005	0.974 to 1.028	0.89	0.43 to 1.72
Borczuk 1995[55]	1448	22.7	74.9	26.0	20.9 to 31.8	75.4	73.1 to 77.6	0.982	0.907 to 1.051	1.06	0.85 to 1.29
Stiell 2001[26]	3121	10.2	89.3	1.2	0.1 to 4.7	98.5	95.5 to 99.8	1.002	0.983 to 1.017	0.79	0.22 to 2.26
Mack 2003[110]	133	0.0	99.1	33.1	25.9 to 41.7	69.7	66.3 to 73.0	0.960	0.843 to 1.062	1.09	0.86 to 1.37
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	8	<0.001	<0.001	14.1	3.9 to 36.0	86.2	67.4 to 95.4	0.997	0.924 to 1.038	1.02	0.68 to 1.33

a Of posterior distribution for Bayesian meta-analyses..
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Age >60 years (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Jeret 1993[107]	712	19.4	94.7	15.7	10.4 to 23.1	94.3	92.4 to 95.9	0.895	0.815 to 0.948	2.73	1.80 to 4.42
Haydel 2000[27]	520	16.7	92.6	17.4	11.2 to 25.5	92.5	90.0 to 92.5	0.894	0.810 to 0.957	2.29	1.51 to 3.50
Ibanez and Arikan 2004[60]	1101	45.8	71.9	42.5	33.4 to 52.6	71.9	69.1 to 71.9	0.799	0.661 to 0.928	1.52	1.18 to 1.90
Mower 2005[62]	13,728	19.0	86.4	20.2	17.5 to 23.2	86.4	85.8 to 86.4	0.924	0.888 to 0.956	1.49	1.28 to 1.73
Stiell 2005[46]	2707	27.3	90.7	24.2	18.7 to 30.3	90.5	89.3 to 90.5	0.838	0.770 to 0.901	2.55	1.90 to 3.30
Ono 2007[63]	1064	48.0	67.6	45.2	34.6 to 57.1	67.7	64.8 to 67.7	0.810	0.635 to 0.969	1.40	1.06 to 1.78
Saboori 2007[67]	682	10.9	94.5	13.6	8.1 to 20.5	94.5	92.6 to 94.5	0.915	0.844 to 0.971	2.45	1.48 to 3.85
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	7	<0.001	<0.001	23.9	14.5 to 36.5	88.0	78.1 to 93.8	0.868	0.785 to 0.925	1.97	1.48 to 2.81

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Vision (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	226	13.0	82.8	8.0	1.2 to 24.4	83.1	77.8 to 88.0	1.104	0.905 to 1.223	0.48	0.07 to 1.51
Cook 1994[100]	107	0.0	92.9	2.5	0.0 to 9.9	93.2	87.8 to 97.0	1.042	0.970 to 1.106	0.37	0.00 to 1.55
Falimirski 2003[58]	331	0.0	98.6	0.6	0.0 to 7.2	98.4	96.4 to 99.5	1.008	0.946 to 1.030	0.39	0.00 to 5.20
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.265	<0.001	2.4	0.0 to 21.4	94.2	70.7 to 99.3	1.033	0.940 to 1.199	0.39	0.00 to 2.49

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Prior neurosurgery (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Arienta 1997[54]	10,000	0.6	100.0	0.9	0.1 to 3.1	99.99	100.0 to 100.0	0.991	0.969 to 0.999	69.80	7.66 to 918.60
Ibanez and Arikan 2004[60]	1101	2.4	99.7	2.0	0.8 to 3.5	99.7	99.3 to 99.9	0.983	0.968 to 0.994	7.13	2.64 to 27.08
Fabbri 2005[57]	7955	3.5	98.0	3.4	2.1 to 5.1	98.0	97.6 to 98.3	0.986	0.968 to 1.000	1.67	1.01 to 2.60
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.231	< 0.001	1.9	0.3 to 5.1	99.8	92.3 to 100.0	0.985	0.969 to 1.030	8.67	0.62 to 308.90

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Motor vehicle collision – pedestrian (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Jeret 1993[107]	712	26.9	87.3	22.9	13.4 to 33.5	87.8	85.1 to 90.2	0.878	0.759 to 0.987	1.88	1.09 to 2.84
Schynoll 1993[118]	264	15.6	96.6	14.9	9.6 to 19.8	96.3	93.8 to 98.1	0.886	0.837 to 0.930	3.88	2.58 to 7.26
Cook 1994[100]	107	0.0	98.6	12.6	4.5 to 19.8	97.7	94.6 to 99.5	0.898	0.826 to 0.965	5.05	2.78 to 17.29
Borczuk 1995[55]	1448	14.3	93.8	17.3	13.7 to 21.4	94.0	92.7 to 95.2	0.880	0.838 to 0.919	2.90	2.17 to 3.74
Stiell 2001[26]	3121	16.9	96.0	15.3	12.0 to 19.1	95.9	95.2 to 96.6	0.883	0.843 to 0.918	3.77	2.84 to 5.03
Ono 2007[63]	1064	10.0	96.6	14.2	9.5 to 19.0	96.6	95.5 to 97.6	0.889	0.839 to 0.933	4.15	2.89 to 6.3
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	6	0.182	< 0.001	15.9	10.9 to 21.3	95.4	91.9 to 97.8	0.882	0.836 to 0.923	3.43	2.27 to 6.45

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Motor vehicle collision – in car (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	302	27.3	53.8	32.2	26.0 to 39.5	55.3	49.4 to 61.0	1.223	1.112 to 1.360	0.72	0.60 to 0.86
Jeret 1993[107]	712	22.4	60.5	27.4	22.4 to 33.0	61.1	57.4 to 64.7	1.187	1.106 to 1.277	0.71	0.59 to 0.83
Schynoll 1993[118]	264	25.0	78.9	15.5	10.7 to 21.1	77.6	72.2 to 82.5	1.089	1.022 to 1.149	0.69	0.52 to 0.91
Cook 1994[100]	107	33.3	85.3	11.4	6.0 to 18.2	83.5	75.7 to 89.6	1.063	0.998 to 1.124	0.68	0.46 to 1.01
Tsai 1994[125]	186	60.0	37.7	50.7	39.4 to 63.0	36.4	29.5 to 43.7	1.353	1.031 to 1.727	0.80	0.63 to 1.0
Borczuk 1995[55]	1448	19.3	65.3	23.7	19.4 to 28.0	65.7	63.2 to 68.2	1.161	1.098 to 1.229	0.69	0.57 to 0.81
Miller 1996[111]	1382	39.3	59.0	30.4	25.4 to 37.3	58.5	55.9 to 61.2	1.188	1.076 to 1.275	0.73	0.62 to 0.89
Stiell 2001[26]	3121	16.1	73.4	18.0	14.6 to 21.6	73.5	71.9 to 75.1	1.117	1.065 to 1.165	0.68	0.55 to 0.82
Mack 2003[110]	133	5.3	95.6	4.0	1.3 to 8.9	94.3	89.3 to 97.5	1.018	0.978 to 1.057	0.68	0.30 to 1.47
Ono 2007[63]	1064	4.0	94.7	3.7	1.6 to 7.6	94.5	93.1 to 95.8	1.018	0.978 to 1.044	0.68	0.30 to 1.39
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	10	< 0.001	< 0.001	17.7	8.7 to 31.0	74.4	57.7 to 86.0	1.108	1.031 to 1.218	0.69	0.53 to 0.86

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Motor vehicle collision with bicycle (intracranial injury – adults)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Borczuk 1995[55]	1448	5.0	98.4	5.0	2.3 to 10.8	98.4	97.6 to 99.0	0.965	0.442 to 2.104	3.19	1.31 to 7.75
Ono 2007[63]	1064	18.0	85.3	18.0	9.6 to 31.1	85.3	83.0 to 87.4	0.961	0.532 to 1.738	1.22	0.67 to 2.25
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.011	< 0.001	10.6	6.4 to 16.9	89.0	87.3 to 90.5	0.963	0.601 to 1.543	1.67	1.01 to 2.75

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Persistent vomiting (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Arienta 1997[54]	10,000	3.9	99.9	3.3	1.2 to 7.0	99.9	99.8 to 100.0	0.968	0.931 to 0.989	35.77	11.13 to 104.50
Stiell 2001[26]	3121	30.3	92.2	29.9	24.7 to 35.7	92.2	91.2 to 93.1	0.760	0.698 to 0.817	3.83	3.06 to 4.76
Stiell 2005[46]	2707	45.9	86.7	44.9	38.5 to 51.3	86.7	85.3 to 88.0	0.636	0.561 to 0.710	3.37	2.82 to 3.99
Mower 2005[62]	13,728	10.0	94.3	10.4	8.5 to 12.6	94.3	93.9 to 94.7	0.950	0.927 to 0.970	1.83	1.48 to 2.24
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	4	< 0.001	< 0.001	16.1	3.0 to 50.7	97.2	69.3 to 99.9	0.871	0.659 to 0.983	5.53	1.33 to 30.12

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale < 15 (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Feuerman 1988[102]	129	62.3	51.3	26.3	21.6 to 31.4	89.9	88.0 to 91.6	0.820	0.761 to 0.876	2.60	2.01 to 3.4
Stein 1990[122]	658	49.1	72.9	25.8	16.3 to 37.3	84.5	79.7 to 88.6	0.878	0.738 to 1.004	1.66	0.98 to 2.7
Livingston 1991[109]	111	40.0	85.4	37.6	25.9 to 50.2	86.8	84.7 to 88.8	0.719	0.573 to 0.855	2.85	1.91 to 4.0
Livingston 1991[109]	60	72.7	71.4	52.9	46.8 to 58.8	82.7	81.3 to 84.1	0.570	0.498 to 0.645	3.05	2.64 to 3.5
Harad 1992[104]	302	21.8	84.2	22.8	15.1 to 32.0	96.6	95.4 to 97.6	0.799	0.704 to 0.879	6.72	4.06 to 10.9
Stein 1992[121]	1538	44.5	76.2	61.0	39.5 to 80.3	72.6	59.5 to 83.4	0.541	0.272 to 0.865	2.21	1.27 to 3.9
Schynoll 1993[118]	264	53.1	85.3	34.7	27.5 to 42.3	80.6	75.2 to 85.2	0.811	0.708 to 0.917	1.78	1.28 to 2.5
Tsai 1994[125]	186	50.0	63.0	50.1	36.4 to 63.9	63.8	55.8 to 71.2	0.784	0.560 to 1.032	1.38	0.95 to 1.9
Borczuk 1995[55]	1448	39.5	85.7	40.0	31.9 to 48.5	85.7	83.8 to 87.6	0.701	0.600 to 0.797	2.80	2.16 to 3.56
Madden 1995[61]	537	78.0	74.9	26.7	13.1 to 44.2	85.7	78.7 to 91.2	0.856	0.651 to 1.033	1.87	0.84 to 3.7
Dunham 1996[101]	2032	64.8	75.4	65.9	61.8 to 69.7	97.7	97.3 to 98.0	0.350	0.310 to 0.391	28.59	24.41 to 33.68
Arienta 1997[54]	9917	42.1	99.6	40.9	31.7 to 50.6	99.5	99.4 to 99.7	0.594	0.496 to 0.687	86.43	59.80 to 125.10
Hsiang 1997[105]	1360	25.6	89.9	42.1	24.2 to 61.5	85.8	78.1 to 91.6	0.678	0.449 to 0.897	2.94	1.49 to 5.6

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Murshid 1998[77]	131	43.3	94.1	51.2	36.2 to 66.0	85.4	80.5 to 89.5	0.572	0.397 to 0.750	3.50	2.26 to 5.3
Stiell 2001[26]	3121	53.1	82.7	74.7	65.7 to 82.6	74.9	70.8 to 78.8	0.337	0.231 to 0.462	2.98	2.44 to 3.6
Mussack 2002[115]	139	47.4	99.2	49.1	40.5 to 57.7	73.0	69.2 to 76.7	0.698	0.577 to 0.823	1.82	1.44 to 2.3
Mack 2003[110]	133	15.8	85.1	63.5	55.3 to 71.3	75.4	73.5 to 77.3	0.484	0.381 to 0.594	2.59	2.21 to 3.0
Tender 2003[123]	255	27.5	81.4	43.4	26.3 to 62.2	98.1	94.9 to 99.5	0.578	0.387 to 0.753	21.98	7.67 to 86.3
Ibanez 2004[60]	1101	20.5	96.7	47.1	30.4 to 64.5	82.7	77.1 to 87.4	0.641	0.428 to 0.850	2.71	1.63 to 4.2
Thiruppathy 2004[124]	381	33.8	80.3	44.6	38.8 to 50.5	76.3	73.9 to 78.6	0.726	0.646 to 0.807	1.88	1.59 to 2.2
Chan 2005[99]	105	69.5	52.2	67.4	57.4 to 76.5	56.2	36.9 to 74.3	0.582	0.379 to 0.945	1.54	1.04 to 2.64
Fabbri 2005[57]	7955	66.4	97.7	60.6	48.2 to 72.2	52.8	41.8 to 63.7	0.746	0.506 to 1.066	1.28	0.94 to 1.75
Biberthaler 2006[98]	1309	32.3	89.6	33.4	24.7 to 42.8	89.6	87.8 to 91.2	0.744	0.638 to 0.841	3.20	2.29 to 4.34
Muller 2007[113]	226	47.6	82.4	42.8	28.2 to 58.3	93.7	88.2 to 97.2	0.613	0.446 to 0.772	6.73	3.26 to 15.9
Ono 2007[63]	1064	36.0	86.8	28.7	22.2 to 36.0	82.2	74.2 to 88.6	0.868	0.761 to 0.994	1.61	1.02 to 2.6
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	25	< 0.001	< 0.001	44.9	37.7 to 51.8	86.7	80.6 to 91.2	0.638	0.557 to 0.722	3.35	2.31 to 5.03

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale < 14 (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Feuerman 1988[102]	129	24.5	89.5	22.0	15.7 to 31.2	92.0	86.2 to 95.5	0.849	0.766 to 0.911	2.81	1.70 to 4.21
Stein 1990[122]	658	21.6	93.2	20.0	15.7 to 25.8	93.4	91.3 to 95.1	0.856	0.799 to 0.900	3.06	2.24 to 4.10
Harad 1992[104]	302	5.5	96.8	12.0	6.9 to 16.7	97.2	95.3 to 98.5	0.905	0.868 to 0.953	4.33	2.53 to 6.5
Stein 1992[121]	1538	17.0	94.1	18.0	14.6 to 21.7	94.4	93.1 to 95.5	0.869	0.831 to 0.905	3.22	2.45 to 4.08
Tsai 1994[125]	186	20.0	88.4	22.9	16.2 to 31.9	91.1	86.1 to 94.5	0.847	0.761 to 0.922	2.60	1.61 to 3.82

continued

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dunham 1996[101]	2032	22.7	95.4	17.3	14.2 to 22.8	95.3	94.3 to 96.1	0.869	0.811 to 0.899	3.65	2.95 to 5.0
Hsiang 1997[105]	1360	8.9	98.2	9.8	7.1 to 12.8	98.1	97.3 to 98.8	0.919	0.890 to 0.946	5.23	3.47 to 8.0
Stiell 2001[26]	3121	17.7	97.7	12.7	10.2 to 17.4	97.4	96.8 to 98.0	0.896	0.847 to 0.921	4.91	3.80 to 7.40
Mack 2003[110]	133	5.3	97.4	12.3	6.2 to 18.4	97.2	94.5 to 98.9	0.902	0.857 to 0.954	4.36	2.66 to 7.3
Tender 2003[123]	255	7.8	94.1	12.1	7.7 to 16.5	97.1	94.4 to 98.5	0.905	0.872 to 0.952	4.19	2.08 to 6.52
Biberthaler 2006[98]	1309	6.5	97.6	10.9	6.8 to 14.3	97.7	96.8 to 98.4	0.912	0.881 to 0.954	4.71	2.88 to 6.5
Muller 2007[113]	226	23.8	94.6	17.6	12.4 to 25.5	94.8	91.7 to 97.0	0.870	0.799 to 0.912	3.44	2.37 to 4.9
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	12	<0.001	<0.001	15.0	11.4 to 18.9	96.0	94.3 to 97.4	0.885	0.853 to 0.915	3.81	2.87 to 4.93

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale decrease (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Madden 1995[61]	537	33.0	93.9	29.1	24.7 to 34.4	94.0	91.5 to 95.9	0.754	0.703 to 0.801	4.84	3.47 to 6.86
Stiell 2001[26]	3121	21.3	98.7	22.0	17.2 to 27.4	98.6	98.2 to 99.0	0.791	0.737 to 0.839	16.11	11.04 to 23.82
Stiell 2005[46]	2707	30.7	91.0	31.2	25.9 to 36.8	91.1	89.9 to 92.2	0.755	0.693 to 0.814	3.50	2.81 to 4.31
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.024	<0.001	27.3	20.8 to 36.7	95.7	83.4 to 98.8	0.763	0.711 to 0.822	6.39	2.05 to 19.33

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Focal neurological deficit (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Cook 1994[100]	107	0.0	98.5	2.8	0.1 to 17.5	99.2	96.4 to 99.9	0.981	0.833 to 1.021	3.44	0.08 to 64.34
Borczuk 1995[55]	1448	3.4	85.9	3.5	1.2 to 7.7	86.0	84.0 to 87.7	1.122	1.070 to 1.161	0.25	0.08 to 0.56
Arienta 1997[54]	10,000	7.1	99.9	6.8	3.6 to 11.5	99.9	99.8 to 100.0	0.933	0.886 to 0.965	71.02	30.16 to 170.3
Falimirski 2003[58]	331	0.0	97.6	1.5	0.1 to 7.2	97.8	95.7 to 99.1	1.007	0.948 to 1.035	0.69	0.03 to 4.09
Ibanez and Arikan 2004[60]	1101	4.8	99.3	4.7	1.6 to 10.3	99.3	98.7 to 99.7	0.960	0.903 to 0.992	6.96	2.00 to 22.04
Chan 2005[99]	105	12.2	87.0	11.5	5.9 to 19.4	91.0	75.4 to 98.0	0.973	0.862 to 1.180	1.28	0.38 to 6.26
Fabbri 2005[57]	7955	54.4	98.8	54.1	49.9 to 58.3	98.8	98.5 to 99.0	0.465	0.422 to 0.507	44.70	36.11 to 56.08
Saboori 2007[67]	682	2.2	100.0	2.5	0.3 to 8.9	99.9	99.5 to 100.0	0.976	0.912 to 0.998	30.36	2.15 to 1392.00
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	8	<0.001	<0.001	6.6	1.2 to 16.9	98.6	95.2 to 99.8	0.95	0.84 to 1.01	9.671	0.663 to 38.950

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Depressed skull fracture (intracranial injury – adults)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Madden 1995[61]	537	13.2	100.0	13.2	7.6 to 21.8	99.9	98.2 to 100.0	0.868	0.512 to 1.471	117.63	7.01 to 1973.44
Miller 1997[29]	2143	2.2	100.0	2.2	0.7 to 6.5	99.98	99.6 to 100.0	0.978	0.822 to 1.165	87.17	4.39 to 1731.74
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.004	0.452	9.1	5.5 to 14.5	99.9	99.6 to 100.0	0.967	0.819 to 1.141	102.15	13.13 to 794.41

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Basal skull fracture (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	264	21.9	94.0	30.8	25.6 to 36.0	94.4	91.2 to 96.9	0.733	0.687 to 0.780	5.85	3.67 to 9.19
Madden 1995[61]	537	28.6	93.9	31.2	26.8 to 35.8	94.2	91.9 to 96.1	0.730	0.686 to 0.774	5.50	3.89 to 7.63
Dunham 1996[101]	2032	27.3	96.6	28.1	24.5 to 31.7	96.7	95.8 to 97.4	0.744	0.708 to 0.779	8.53	6.69 to 10.76
Arienta 1997[54]	10,000	0.6	100.0	4.5	1.7 to 8.2	100.0	100.0 to 100.0	0.955	0.918 to 0.983	13,090	429.40 to 77,610
Stiell 2001[26]	3121	30.3	95.4	30.1	26.6 to 33.8	95.4	94.6 to 96.1	0.733	0.696 to 0.769	6.53	5.40 to 7.82
Ibanez 2004[60]	1101	19.3	97.9	24.9	20.7 to 28.6	98.1	97.2 to 98.8	0.766	0.731 to 0.806	13.42	9.03 to 19.51
Fabbri 2005[57]	7955	16.6	99.9	14.1	11.7 to 16.7	99.9	99.8 to 99.9	0.860	0.834 to 0.884	129.10	64.37 to 256.80
Stiell 2005[46]	2707	29.9	96.4	28.7	25.4 to 32.3	96.4	95.6 to 97.1	0.740	0.704 to 0.773	8.01	6.49 to 9.85
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	8	< 0.001	< 0.001	21.1	8.4 to 33.9	98.4	90.5 to 100.0	0.80	0.72 to 0.92	54.070	3.594 to 353.700

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any seizure (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	264	3.1	96.1	4.7	3.0 to 7.0	96.5	93.8 to 98.3	0.987	0.972 to 1.008	1.37	0.85 to 2.22
Cook 1994[100]	107	0.0	97.2	3.9	1.7 to 6.8	97.7	93.7 to 99.4	0.985	0.970 to 1.007	1.67	0.89 to 4.18
Arienta 1997[54]	10,000	0.6	100.0	0.4	0.0 to 1.8	100.0	100.0 to 100.0	0.996	0.982 to 1.000	29.56	2.39 to 501.40
Haydel 2000[27]	520	11.1	95.9	5.1	3.6 to 7.4	95.8	93.8 to 97.3	0.989	0.971 to 1.009	1.25	0.84 to 1.79
Falimirski 2003[58]	331	2.5	99.3	2.3	0.8 to 4.1	99.3	98.1 to 99.9	0.984	0.970 to 0.996	3.26	1.47 to 11.16
Ibanez and Arikan 2004[60]	1101	1.2	99.4	2.1	0.8 to 3.7	99.5	98.9 to 99.8	0.985	0.970 to 0.997	3.69	1.61 to 8.85
Chan 2005[99]	105	3.7	95.7	3.9	1.6 to 7.2	97.8	91.1 to 99.7	0.986	0.971 to 1.028	1.70	0.69 to 6.54

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Mower 2005[62]	13,728	5.0	96.1	5.0	3.8 to 6.4	96.1	95.7 to 96.4	0.989	0.974 to 1.002	1.27	0.96 to 1.66
Stiell 2005[46]	1822	4.3	98.1	3.6	2.4 to 4.9	98.1	97.4 to 98.7	0.983	0.970 to 0.994	1.89	1.29 to 2.79
Saboori 2007[67]	682	0.0	99.7	1.6	0.4 to 3.3	99.7	99.1 to 99.9	0.987	0.971 to 0.998	5.19	1.72 to 21.4
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	10	0.262	< 0.001	2.8	1.1 to 5.1	99.0	96.2 to 99.7	0.984	0.970 to 0.996	2.59	1.20 to 6.40

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any loss of consciousness (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Nelson 1992[116]	131	90.0	21.6	88.0	74.6 to 95.7	21.8	15.0 to 29.8	0.553	0.201 to 1.203	1.12	0.95 to 1.3
Schynoll 1993[118]	264	50.0	66.8	50.4	35.3 to 65.4	66.8	60.7 to 72.6	0.742	0.519 to 0.979	1.52	1.04 to 2.1
Cook 1994[100]	107	44.4	48.5	56.0	31.0 to 77.0	50.1	40.4 to 59.7	0.877	0.467 to 1.413	1.12	0.62 to 1.6
Moran 1994[112]	200	100.0	55.7	78.0	56.3 to 93.8	55.0	48.0 to 61.8	0.402	0.114 to 0.795	1.72	1.24 to 2.2
Borczuk 1995[55]	1448	77.3	36.8	77.2	69.6 to 83.8	36.8	34.3 to 39.4	0.618	0.439 to 0.835	1.22	1.09 to 1.3
Madden 1995[61]	537	94.5	30.9	91.8	85.5 to 96.2	30.6	26.5 to 34.9	0.267	0.121 to 0.479	1.32	1.21 to 1.4
Miller 1996[111]	1382	65.5	39.1	66.7	56.6 to 75.7	39.2	36.5 to 41.8	0.851	0.617 to 1.117	1.10	0.93 to 1.25
Arienta 1997[54]	10,000	3.9	98.7	3.9	1.8 to 7.6	98.7	98.5 to 98.9	0.973	0.936 to 0.995	3.10	1.36 to 6.1
Sharma 2001[120]	39	44.4	19.0	58.1	36.4 to 76.6	31.3	15.4 to 50.7	1.324	0.696 to 2.958	0.85	0.52 to 1.2
Stiell 2001[26]	3121	52.0	54.6	52.4	46.4 to 58.4	54.6	52.8 to 56.4	0.872	0.760 to 0.987	1.15	1.02 to 1.30
Mack 2003[110]	133	42.1	72.8	70.7	60.8 to 79.6	70.0	67.2 to 72.8	0.419	0.291 to 0.562	2.36	1.98 to 2.75
Ibanez 2004[60]	1101	73.5	70.2	88.5	81.0 to 93.9	14.3	5.4 to 28.7	0.800	0.356 to 2.220	1.03	0.92 to 1.2
Chan 2005[99]	105	87.8	8.7	53.3	49.1 to 57.5	82.4	81.6 to 83.3	0.566	0.516 to 0.618	3.04	2.76 to 3.3
Fabbri 2005[57]	7955	53.7	82.5	63.1	59.9 to 66.1	53.1	52.2 to 53.9	0.696	0.638 to 0.756	1.34	1.27 to 1.4

continued

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Mower 2005[62]	13,728	63.0	53.1	53.7	47.4 to 60.0	53.0	51.0 to 54.9	0.874	0.754 to 0.999	1.14	1.00 to 1.3
Stiell 2005[46]	2707	53.2	52.9	43.1	25.7 to 61.9	72.8	64.4 to 80.2	0.782	0.526 to 1.032	1.58	0.93 to 2.5
Saboori 2007[67]	682	8.7	88.4	12.8	5.6 to 23.0	88.5	85.9 to 90.8	0.985	0.869 to 1.071	1.11	0.48 to 2.1
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	17	< 0.001	< 0.001	59.9	43.0 to 75.8	58.0	39.5 to 74.1	0.698	0.532 to 0.871	1.41	1.14 to 1.84

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any headache (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	228	40.9	26.7	61.2	37.5 to 79.2	29.6	23.5 to 36.4	1.311	0.686 to 2.288	0.87	0.52 to 1.15
Cook 1994[100]	107	75.0	41.7	64.8	46.3 to 81.9	42.4	33.3 to 51.9	0.830	0.436 to 1.277	1.13	0.81 to 1.46
Borczuk 1995[55]	1448	50.4	61.2	48.7	41.2 to 57.3	61.1	58.5 to 63.7	0.841	0.697 to 0.965	1.25	1.05 to 1.49
Holmes 1997[59]	261	45.7	75.2	38.1	27.3 to 53.6	74.2	68.5 to 79.5	0.837	0.623 to 0.972	1.47	1.07 to 2.22
Haydel 2000[27]	520	33.3	77.1	31.1	21.7 to 44.1	76.9	73.1 to 80.4	0.899	0.727 to 1.018	1.34	0.94 to 2.0
Falimirski 2003[58]	331	22.5	85.2	21.7	13.7 to 33.0	84.8	80.6 to 88.5	0.927	0.790 to 1.018	1.41	0.91 to 2.30
Mack 2003[110]	133	31.6	79.8	28.8	17.6 to 44.5	79.1	71.7 to 85.4	0.907	0.709 to 1.042	1.35	0.86 to 2.26
Ibanez 2004[60]	1101	69.9	45.6	65.9	56.4 to 75.5	45.4	42.4 to 48.5	0.752	0.535 to 0.965	1.21	1.03 to 1.40
Chan 2005[99]	105	43.9	69.6	42.6	33.1 to 52.6	66.8	52.9 to 80.0	0.866	0.680 to 1.074	1.27	0.90 to 2.12
Fabbri 2005[57]	7955	17.2	83.4	18.0	14.8 to 21.7	83.5	82.6 to 84.3	0.982	0.937 to 1.023	1.09	0.89 to 1.32
Stiell 2005[46]	1822	37.1	64.8	39.0	30.2 to 46.9	64.9	62.7 to 67.2	0.938	0.818 to 1.080	1.11	0.86 to 1.34
Ono 2007[63]	1064	38.0	85.8	29.1	17.3 to 43.9	85.3	83.0 to 87.4	0.831	0.657 to 0.972	1.99	1.16 to 3.10
Saboori to 2007[67]	682	4.3	85.5	14.0	5.6 to 22.0	85.9	83.1 to 88.5	0.999	0.911 to 1.105	1.01	0.39 to 1.57

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	13	< 0.001	< 0.001	36.8	25.5 to 50.5	70.3	57.3 to 79.8	0.901	0.792 to 1.005	1.23	0.99 to 1.55

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Anterograde or post-trauma amnesia (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	239	27.3	91.2	18.6	12.0 to 26.2	90.6	86.7 to 93.7	0.900	0.840 to 0.950	1.95	1.53 to 2.53
Arienta 1997[54]	10,000	2.6	98.6	3.1	1.4 to 5.8	98.6	98.3 to 98.8	0.984	0.956 to 1.000	2.11	0.97 to 4.08
Stiell 2001[26]	3121	40.2	76.8	39.7	34.3 to 45.3	76.8	75.3 to 78.4	0.785	0.712 to 0.856	1.71	1.47 to 1.98
Ibanez and Arikan 2004[60]	1101	21.7	91.1	18.2	13.7 to 23.0	90.8	89.0 to 92.4	0.902	0.853 to 0.945	1.97	1.54 to 2.5
Stiell 2005[46]	1822	23.7	85.0	27.1	22.3 to 32.2	85.2	83.6 to 86.8	0.855	0.800 to 0.908	1.84	1.53 to 2.16
Saboori 2007[67]	682	8.7	93.7	12.2	7.7 to 17.4	94.0	92.1 to 95.5	0.935	0.888 to 0.975	2.01	1.39 to 2.76
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	6	< 0.001	< 0.001	16.2	6.8 to 30.9	91.9	83.2 to 96.4	0.912	0.825 to 0.972	1.95	1.48 to 2.62

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined vomiting (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	261	25.0	69.9	27.1	15.5 to 41.1	70.9	64.7 to 76.5	1.028	0.824 to 1.223	0.93	0.52 to 1.48
Holmes 1997[59]	261	14.3	97.8	14.2	7.1 to 24.9	97.4	95.0 to 98.9	0.882	0.773 to 0.955	5.36	2.26 to 13.71
Miller 1997[29]	2143	15.2	95.0	15.6	10.7 to 21.7	95.0	93.9 to 95.9	0.889	0.825 to 0.941	3.10	2.04 to 4.52

continued

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Haydel 2000[27]	520	11.1	91.1	15.4	7.7 to 25.7	91.3	88.6 to 93.6	0.926	0.814 to 1.016	1.78	0.85 to 3.16
Mussack 2002[115]	139	21.1	91.7	20.6	10.5 to 35.0	91.9	86.5 to 95.7	0.866	0.710 to 0.982	2.54	1.16 to 5.40
Ibanez and Arikan 2004[60]	1101	22.9	93.2	21.9	14.8 to 30.5	93.2	91.6 to 94.6	0.839	0.746 to 0.915	3.21	2.08 to 4.8
Chan 2005[99]	105	45.1	69.6	41.9	32.0 to 52.5	73.7	54.9 to 87.6	0.790	0.613 to 1.079	1.59	0.89 to 3.41
Fabbri 2005[57]	7955	16.1	97.4	15.9	13.0 to 19.1	97.4	97.0 to 97.8	0.863	0.830 to 0.893	6.14	4.84 to 7.75
Stiell 2005[46]	1822	20.6	90.1	20.7	14.2 to 28.5	90.1	88.7 to 91.5	0.880	0.794 to 0.954	2.10	1.41 to 2.97
Saboori 2007[67]	682	17.4	95.1	17.4	9.9 to 27.3	95.1	93.3 to 96.6	0.870	0.766 to 0.949	3.52	1.90 to 6.20
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	10	<0.001	<0.001	20.2	13.7 to 28.3	92.2	85.8 to 95.9	0.868	0.794 to 0.935	2.58	1.52 to 4.49

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined or mixed amnesia (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Borczuk 1995[55]	1448	31.1	81.7	28.9	22.0 to 36.7	81.5	79.3 to 83.5	0.874	0.776 to 0.960	1.55	1.17 to 2.02
Miller 1996[111]	1382	34.5	60.9	40.1	29.4 to 53.0	61.4	58.7 to 64.0	0.977	0.759 to 1.159	1.04	0.75 to 1.40
Stiell 2001[26]	3121	92.9	13.3	93.2	89.8 to 95.7	13.4	12.2 to 14.6	0.513	0.318 to 0.775	1.08	1.03 to 1.11
Mussack 2002[115]	139	63.2	40.8	68.7	51.9 to 80.6	42.1	33.9 to 50.5	0.739	0.486 to 1.149	1.19	0.90 to 1.4
Mack 2003[110]	133	15.8	79.8	22.6	10.5 to 36.8	80.7	73.4 to 86.8	0.957	0.804 to 1.119	1.19	0.56 to 1.88
Chan 2005[99]	105	9.8	87.0	11.2	5.8 to 18.7	89.6	79.1 to 95.5	0.990	0.916 to 1.115	1.09	0.49 to 2.20
Fabbri 2005[57]	7955	67.2	57.3	66.0	61.6 to 70.1	57.3	56.1 to 58.4	0.593	0.522 to 0.672	1.55	1.43 to 1.65

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	7	< 0.001	< 0.001	50.9	24.5 to 77.9	60.0	35.3 to 79.7	0.815	0.579 to 1.008	1.27	0.98 to 1.59

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Severe or persistent headache (intracranial injury – adults)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Miller 1997[29]	2143	54.3	69.2	54.3	46.0 to 62.5	69.2	67.2 to 71.2	0.659	0.512 to 0.849	1.77	1.39 to 2.24
Mower 2005[62]	13,728	12.0	82.6	12.0	10.1 to 14.3	82.6	82.0 to 83.3	1.065	0.991 to 1.144	0.69	0.57 to 0.84

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	< 0.001	< 0.001	19.4	16.8 to 22.2	80.5	79.9 to 81.2	1.028	0.959 to 1.101	1.00	0.86 to 1.16

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Retrograde amnesia (intracranial injury – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schynoll 1993[118]	240	50.0	68.3	49.6	43.6 to 56.6	68.9	62.5 to 74.6	0.732	0.637 to 0.832	1.60	1.31 to 1.95
Stiell 2001[26]	3121	38.2	80.7	44.0	39.1 to 48.1	80.9	79.4 to 82.3	0.692	0.641 to 0.754	2.30	2.01 to 2.6
Fabbri 2005[57]	7955	33.9	95.4	33.4	29.5 to 37.4	95.4	94.9 to 95.8	0.698	0.656 to 0.739	7.21	6.14 to 8.41
Stiell 2005[46]	2707	54.5	71.1	49.4	44.2 to 55.3	71.0	69.2 to 72.7	0.713	0.629 to 0.787	1.70	1.51 to 1.93

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	4	< 0.001	< 0.001	44.3	36.9 to 55.2	81.6	56.7 to 91.6	0.687	0.635 to 0.848	2.41	1.21 to 4.55

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Radiological skull fracture (intracranial injury – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Rosenorn 1991[117]	1876	11.1	98.7	16.5	2.5 to 39.9	98.7	98.1 to 99.2	0.846	0.609 to 0.988	13.13	1.88 to 33.53
Shackford 1992[119]	423	60.8	72.1	60.6	50.7 to 70.0	72.8	67.8 to 77.5	0.542	0.409 to 0.686	2.24	1.74 to 2.83
Moran 1994[112]	200	62.5	97.9	52.4	23.9 to 81.5	97.7	95.3 to 99.2	0.487	0.190 to 0.779	27.94	8.50 to 72.56
Dunham 1996[101]	2032	27.3	97.5	33.9	26.5 to 41.9	97.5	96.7 to 98.1	0.678	0.597 to 0.754	13.72	9.45 to 19.37
Mack 2003[110]	133	0.0	97.4	7.3	0.3 to 21.5	97.7	94.6 to 99.5	0.949	0.803 to 1.030	4.41	0.14 to 17.68
Chan 2005[99]	92	54.9	100.0	53.6	42.2 to 65.0	97.4	90.9 to 99.9	0.476	0.358 to 0.597	105.10	5.84 to 385.30
Ono 2007[63]	1064	48.0	99.4	45.8	32.2 to 59.6	99.3	98.7 to 99.7	0.546	0.407 to 0.683	72.05	30.90 to 155.10
Saboori 2007[67]	682	4.3	98.4	7.2	1.6 to 16.5	98.4	97.4 to 99.2	0.942	0.848 to 1.001	5.13	0.95 to 13.76
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	8	< 0.001	< 0.001	29.8	9.8 to 55.9	97.4	94.2 to 99.2	0.720	0.455 to 0.923	14.26	3.68 to 38.43

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Post-trauma seizure (intracranial injury – adults)

Study	*n*	Observed estimates		Fixed-effects estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Stiell 2001[26]	3121	0.4	99.9	0.4	0.1 to 2.7	99.9	99.7 to 100.0	0.997	0.141 to 7.052	3.76	0.39 to 36.04
Fabbri 2005[57]	7955	8.5	99.3	8.5	6.4 to 11.1	99.3	99.1 to 99.5	0.921	0.841 to 1.009	12.84	8.67 to 19.02
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.002	0.002	7.9	6.0 to 10.4	99.4	99.2 to 99.5	0.921	0.841 to 1.009	12.39	8.41 to 18.24

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Need for neurosurgery in adults

Fall – any (neurosurgery – adults)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	302	18.2	81.8	18.2	4.6 to 50.7	81.8	76.9 to 85.8	1.000	0.285 to 3.508	1.00	0.28 to 3.58
Miller 1996[111]	1382	0.0	73.1	16.7	1.0 to 80.6	73.1	70.7 to 75.4	1.140	0.091 to 14.319	0.62	0.05 to 7.79
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.952	0.002	17.9	5.2 to 46.1	74.4	72.3 to 76.5	1.027	0.334 to 3.159	0.91	0.29 to 2.83

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Assault (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	63.6	83.2	63.6	33.9 to 85.7	83.2	78.4 to 87.0	0.437	0.200 to 0.957	3.78	2.26 to 6.32

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Motor vehicle collision – pedestrian (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	0.0	85.9	4.5	0.3 to 44.8	85.9	81.4 to 89.5	1.111	0.969 to 1.274	0.32	0.02 to 4.91

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Motor vehicle collision – in car (neurosurgery – adults)

Study	*n*	Observed estimates		Fixed-effects estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	302	0.0	55.7	16.7	0.3 to 44.8	55.7	49.9 to 61.3	1.715	0.114 to 25.772	0.10	0.01 to 1.54
Miller 1996[111]	1382	0.0	59.0	4.5	1.0 to 80.6	59.0	56.4 to 61.6	1.412	0.112 to 17.735	0.41	0.03 to 5.11
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.498	0.291	8.5	1.2 to 42.5	58.4	56.1 to 60.8	1.546	0.243 to 9.826	0.21	0.03 to 1.36

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale <15 (neurosurgery – adults)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Feuerman 1988[102]	129	75.0	47.1	62.1	34.7 to 87.2	47.9	39.2 to 56.7	0.790	0.266 to 1.419	1.19	0.65 to 1.76
Stein 1990[122]	658	36.8	69.2	41.1	22.7 to 60.7	69.3	65.6 to 72.8	0.851	0.568 to 1.122	1.34	0.73 to 2.01
Borczuk 1995[55]	1448	90.9	84.2	73.8	49.9 to 93.2	84.2	82.3 to 86.1	0.311	0.082 to 0.596	4.67	3.11 to 6.10
Gomez 1996[103]	2484	53.3	95.2	53.8	37.7 to 69.5	95.2	94.3 to 96.0	0.486	0.320 to 0.655	11.24	7.60 to 15.41
Arienta 1997[54]	9917	62.5	99.3	61.5	42.1 to 78.3	99.3	99.1 to 99.4	0.388	0.219 to 0.583	86.30	56.30 to 123.10
Hsiang 1997[105]	1360	38.1	87.3	40.7	27.4 to 54.6	87.3	85.5 to 89.1	0.679	0.520 to 0.833	3.21	2.12 to 4.46
Thiruppathy 2004[124]	381	33.3	75.4	37.8	22.2 to 54.7	75.6	70.9 to 79.8	0.823	0.596 to 1.041	1.55	0.88 to 2.4
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	7	0.026	<0.001	53.1	34.8 to 73.1	86.8	62.3 to 96.2	0.546	0.310 to 0.881	4.00	1.24 to 14.61

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale < 14 (neurosurgery – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Feuerman 1988[102]	129	25.0	84.3	14.0	6.8 to 24.9	85.8	79.0 to 91.2	1.001	0.856 to 1.143	0.99	0.39 to 2.24
Stein 1990[122]	658	15.8	90.8	17.1	9.9 to 26.5	90.9	88.5 to 92.9	0.912	0.806 to 1.000	1.88	1.00 to 3.20
Gomez 1996[103]	2484	40.0	98.7	34.8	22.8 to 48.5	98.6	98.1 to 99.0	0.662	0.522 to 0.784	25.06	14.50 to 42.66
Hsiang 1997[105]	1360	21.4	97.3	27.0	18.9 to 36.3	97.1	96.2 to 97.9	0.752	0.654 to 0.837	9.42	5.72 to 15.24
Thiruppathy 2004[124]	381	18.5	89.8	16.6	9.4 to 26.1	90.2	86.9 to 92.9	0.925	0.813 to 1.020	1.70	0.85 to 3.09
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	0.271	< 0.001	21.0	10.0 to 33.4	94.3	84.9 to 98.0	0.839	0.684 to 1.042	3.67	0.75 to 15.81

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Focal neurological deficit (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Feuerman 1988[102]	50.0	93.7	50.0	20.0 to 80.0	93.7	90.7 to 95.8	0.534	0.125 to 2.272	7.93	1.86 to 33.79

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Depressed skull fracture (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Miller 1997[29]	60.0	100.0	60.0	20.0 to 90.0	99.98	99.6 to 100.0	0.400	0.137 to 1.171	2565.6	146.6 to 44,909

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Any loss of consciousness (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Miller 1996[111]	0.0	38.7	16.7	1.0 to 80.6	38.7	36.1 to 41.3	2.156	0.103 to 44.998	0.27	0.01 to 5.67

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Any headache (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Holmes 1997[59]	25.0	78.5	25.0	3.4 to 76.2	78.5	73.0 to 83.0	0.956	0.098 to 9.368	1.16	0.12 to 11.38

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Undefined vomiting (neurosurgery – adults)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Holmes 1997[59]	264	25.0	98.1	25.0	3.4 to 76.2	98.1	95.5 to 99.2	0.765	0.245 to 2.387	13.00	1.52 to 111.28
Miller 1997[29]	2143	20.0	94.3	20.0	2.7 to 69.1	94.3	93.3 to 95.2	0.848	0.318 to 2.262	3.53	0.49 to 25.29
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.858	0.015	22.3	5.6 to 58.1	94.6	93.6 to 95.4	0.811	0.386 to 1.706	6.41	1.50 to 27.33

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined or mixed amnesia (neurosurgery – adults)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Miller 1996[111]	0.0	61.1	16.7	1.0 to 80.6	61.1	58.5 to 63.7	1.363	0.065 to 28.451	0.43	0.02 to 8.95

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Severe or persistent headache (neurosurgery – all ages)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Miller 1997[29]	20.0	67.7	20.0	2.7 to 69.1	67.7	65.7 to 69.6	1.182	0.132 to 10.596	0.62	0.07 to 5.55

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Radiological skull fracture (neurosurgery – adults)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Murshid 1994[114]	566	57.1	89.3	39.5	30.1 to 49.8	90.2	87.6 to 92.1	0.671	0.549 to 0.791	4.00	2.54 to 6.12
Hung 1996[106]	7000	37.8	90.2	39.1	34.7 to 43.5	90.1	89.4 to 90.8	0.676	0.627 to 0.725	3.96	3.45 to 4.52
Stein 1992[121]	1538	60.3	93.5	51.4	41.5 to 65.5	93.3	91.9 to 94.6	0.520	0.369 to 0.631	7.79	5.50 to 10.82
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.004	<0.001	43.1	31.0 to 58.6	91.3	87.3 to 94.1	0.623	0.444 to 0.788	4.99	2.48 to 9.48

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Appendix 6

Individual clinical characteristics in children and infants – data for meta-analysis

Intracranial injury in children

Intoxication (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Haydel 2003[88]	175	7.1	93.8	3.4	1.3 to 7.0	94.4	90.2 to 97.2	1.022	0.977 to 1.078	0.61	0.19 to 1.63
Dunning 2006[30]	22,772	4.6	99.8	4.5	2.5 to 7.3	99.8	99.8 to 99.9	0.957	0.929 to 0.976	28.10	14.69 to 50.93
Oman 2006[91]	1666	4.0	95.0	3.4	1.4 to 6.9	95.1	93.9 to 96.1	1.015	0.978 to 1.040	0.70	0.28 to 1.5
Atabaki 2008[81]	1000	1.5	99.1	3.9	2.3 to 6.0	99.1	98.4 to 99.6	0.970	0.948 to 0.988	4.57	1.92 to 11.25
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	4	0.689	< 0.001	3.8	1.8 to 6.4	98.6	90.2 to 99.8	0.976	0.946 to 1.072	2.72	0.29 to 26.06

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Fall – any (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	249	26.7	53.4	28.2	18.1 to 39.9	53.0	49.0 to 57.0	1.360	1.076 to 1.647	0.60	0.36 to 0.90
Boran 2006[128]	421	40.5	60.2	44.5	32.1 to 57.7	57.7	54.0 to 61.6	0.965	0.707 to 1.228	1.06	0.72 to 1.44
Dunning 2006[30]	22,772	11.7	46.5	12.4	8.7 to 16.5	46.6	45.9 to 47.2	1.883	1.791 to 1.966	0.23	0.16 to 0.31
Atabaki 2008[81]	1000	61.5	56.8	52.7	40.9 to 64.8	58.6	55.7 to 61.3	0.809	0.597 to 1.023	1.27	0.97 to 1.59
Guzel 2009[87]	337	40.3	61.5	43.1	32.9 to 53.7	57.4	53.8 to 61.7	0.993	0.777 to 1.223	1.02	0.73 to 1.34

continued

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	< 0.001	< 0.001	34.7	17.0 to 56.5	54.7	49.1 to 60.6	1.206	0.726 to 1.683	0.78	0.34 to 1.41

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Fall from a height (intracranial injury – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Reed 2005[136]	39	30.0	86.2	30.0	10.0 to 62.4	86.2	68.5 to 94.7	0.812	0.312 to 2.116	2.18	0.59 to 8.09
Dunning 2006[30]	22,772	19.6	80.2	19.6	15.3 to 24.6	80.2	79.7 to 80.7	1.003	0.791 to 1.271	0.99	0.78 to 1.26

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.423	0.421	20.0	15.8 to 25.0	80.2	79.7 to 80.7	0.991	0.787 to 1.247	1.01	0.80 to 1.28

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Dizziness (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Davis 1994[129]	168	0.0	98.1	5.6	0.1 to 16.2	96.4	90.9 to 99.0	0.986	0.862 to 1.054	1.35	0.05 to 8.42
Reed 2005[136]	39	0.0	93.1	5.1	0.6 to 12.4	93.0	85.7 to 98.1	1.018	0.920 to 1.117	0.74	0.11 to 3.57
Atabaki 2008[81]	1000	7.7	89.9	5.3	1.8 to 11.6	90.3	88.3 to 92.2	1.048	0.977 to 1.095	0.55	0.18 to 1.23

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.881	0.012	5.2	0.6 to 13.3	93.5	85.7 to 98.5	1.014	0.910 to 1.109	0.79	0.11 to 4.30

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Coagulopathy (intracranial injury – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dunning 2006[30]	22,772	0.0	99.9	0.2	0.001 to 2.8	99.9	99.9 to 100.0	0.999	0.063 to 15.930	2.86	0.17 to 47.88
Oman 2006[91]	1666	7.0	99.0	7.0	3.8 to 12.6	99.0	98.4 to 99.4	0.939	0.511 to 1.726	7.00	3.19 to 15.37
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.010	< 0.001	5.8	3.2 to 10.5	99.7	99.6 to 99.8	0.942	0.520 to 1.706	6.56	3.08 to 14.00

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Assault (intracranial injury – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dunning 2006[30]	22,772	3.6	95.9	3.6	1.9 to 6.5	95.9	95.6 to 96.1	1.006	0.547 to 1.848	0.87	0.47 to 1.60
Ramundo 1995[135]	261	2.2	92.6	2.2	0.3 to 14.2	92.6	88.3 to 95.4	1.056	0.152 to 7.337	0.30	0.04 to 2.20
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.648	0.017	3.4	1.9 to 6.0	95.9	95.6 to 96.1	1.010	0.565 to 1.805	0.79	0.44 to 1.42

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Vision (intracranial injury – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dunning 2006[30]	22,772	1.4	98.9	1.4	0.5 to 3.7	98.9	98.8 to 99.1	0.996	0.377 to 2.636	1.35	0.50 to 3.59
Guzel 2009[87]	337	17.9	98.9	17.9	10.5 to 28.9	98.9	96.6 to 99.6	0.830	0.497 to 1.386	16.12	4.68 to 55.51

continued

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	< 0.001	0.933	9.1	5.6 to 14.5	98.9	98.8 to 99.1	0.864	0.549 to 1.360	3.51	1.63 to 7.57

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Prior neurosurgery (intracranial injury – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dunning 2006[30]	0.7	99.9	0.7	0.2 to 2.8	99.9	99.8 to 99.9	0.994	0.984 to 1.004	5.93	1.42 to 24.81

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Motor vehicle collision – pedestrian (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Harad 1992[104]	302	18.2	87.4	18.4	10.9 to 27.0	87.8	83.4 to 91.4	0.930	0.826 to 1.029	1.50	0.83 to 2.55
Tsai 1994[125]	186	5.0	91.8	13.7	3.0 to 23.8	91.6	86.6 to 95.4	0.945	0.819 to 1.072	1.58	0.35 to 3.90
Boran 2006[128]	421	43.2	80.2	28.9	13.2 to 51.8	80.8	76.7 to 84.6	0.883	0.597 to 1.088	1.48	0.67 to 2.80
Dunning 2006[30]	22,772	28.1	98.7	27.3	22.2 to 32.8	98.7	98.5 to 98.8	0.737	0.681 to 0.788	20.79	16.46 to 25.85
Atabaki 2008[81]	1000	4.6	91.2	11.5	3.0 to 23.4	91.2	89.3 to 92.9	0.969	0.837 to 1.067	1.34	0.34 to 2.87
Guzel 2009[87]	337	23.9	88.1	20.7	14.5 to 31.7	88.5	84.4 to 91.9	0.894	0.768 to 0.983	1.84	1.11 to 3.1
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	6	< 0.001	< 0.001	19.4	9.0 to 30.2	91.9	81.7 to 96.6	0.883	0.754 to 1.043	2.32	0.75 to 6.56

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Motor vehicle collision – in car (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	261	51.1	76.4	31.7	19.5 to 53.4	74.6	68.5 to 80.3	0.918	0.611 to 1.094	1.27	0.76 to 2.36
Boran 2006[128]	421	13.5	83.9	19.2	10.0 to 26.9	84.3	80.5 to 87.7	0.959	0.871 to 1.075	1.23	0.62 to 1.76
Dunning 2006[30]	22,772	5.0	99.2	4.6	2.6 to 7.2	99.2	99.1 to 99.3	0.962	0.935 to 0.982	5.87	3.20 to 9.43
Atabaki 2008[81]	1000	10.8	78.9	20.8	9.2 to 29.8	79.4	76.7 to 81.9	0.999	0.882 to 1.152	1.01	0.44 to 1.47
Guzel 2009[87]	337	7.5	96.3	9.2	4.8 to 13.8	96.4	94.0 to 98.1	0.942	0.901 to 0.989	2.68	1.26 to 4.56
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	<0.001	<0.001	15.2	5.6 to 31.7	90.0	67.9 to 98.4	0.947	0.870 to 1.065	1.99	0.82 to 4.30

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Motor vehicle collision with bicycle (intracranial injury – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dunning 2006[30]	15.3	96.7	15.3	11.5 to 20.0	96.7	96.5 to 96.9	0.876	0.833 to 0.921	4.63	3.49 to 6.15

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Persistent vomiting (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Da Dalt 2006[83]	3803	14.3	94.4	17.8	7.2 to 32.7	94.4	93.6 to 95.0	0.871	0.713 to 0.984	3.15	1.26 to 5.89
Dunning 2006[30]	22,772	29.2	94.1	28.7	23.7 to 34.1	94.1	93.7 to 94.4	0.758	0.701 to 0.812	4.83	3.96 to 5.78
Oman 2006[91]	1666	24.0	89.0	23.6	17.3 to 30.9	89.1	87.5 to 90.6	0.857	0.774 to 0.930	2.18	1.55 to 3.0
Kupperman 2009[90]	31,292	18.8	92.4	19.0	14.7 to 23.8	92.4	92.1 to 92.7	0.877	0.824 to 0.923	2.51	1.93 to 3.16

continued

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	4	0.028	< 0.001	22.1	10.7 to 40.6	92.9	87.4 to 96.8	0.840	0.635 to 0.969	3.14	1.30 to 8.05

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale <15 (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Chan 1990[212]	418	23.1	95.6	26.2	10.2 to 48.5	95.5	93.2 to 97.2	0.774	0.540 to 0.941	5.78	2.17 to 12.36
Dietrich 1993[84]	253	75.0	77.0	73.0	58.3 to 84.9	77.2	71.4 to 82.4	0.351	0.197 to 0.543	3.18	2.35 to 4.30
Ramundo 1995[135]	259	76.7	70.8	75.3	62.0 to 86.1	71.2	65.0 to 76.9	0.348	0.196 to 0.539	2.60	1.99 to 3.37
Stein 1995[139]	751	40.4	80.1	41.3	31.9 to 51.2	80.3	77.1 to 83.2	0.731	0.606 to 0.852	2.09	1.56 to 2.73
Mandera 2000[133]	166	61.8	70.4	62.1	50.5 to 72.6	71.6	62.3 to 79.8	0.531	0.377 to 0.713	2.18	1.55 to 3.16
Simon 2001[138]	569	17.9	88.7	19.8	12.4 to 29.0	88.9	85.9 to 91.5	0.902	0.796 to 0.991	1.79	1.06 to 2.84
Reed 2005[136]	39	90.0	82.8	77.4	52.8 to 93.7	82.3	67.1 to 92.3	0.277	0.079 to 0.577	4.27	2.22 to 9.9
Dunning 2006[30]	22,772	55.5	98.5	54.8	49.0 to 60.5	98.5	98.3 to 98.6	0.459	0.401 to 0.518	36.04	30.97 to 41.7
Oman 2006[91]	1666	68.8	82.0	68.4	60.5 to 75.7	82.0	80.0 to 83.9	0.386	0.296 to 0.483	3.80	3.24 to 4.4
Atabaki 2008[81]	1000	29.2	86.2	30.9	20.7 to 42.2	86.3	84.0 to 88.4	0.801	0.668 to 0.922	2.26	1.47 to 3.2
Guzel 2009[87]	337	10.4	97.0	12.3	6.2 to 21.2	97.0	94.6 to 98.5	0.905	0.813 to 0.972	4.09	1.67 to 9.7
Kupperman 2009[90]	31,694	26.6	97.4	26.6	21.6 to 31.9	97.4	97.2 to 97.6	0.754	0.699 to 0.804	10.30	8.32 to 12.5

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	12	< 0.001	< 0.001	46.3	29.6 to 64.2	89.6	81.1 to 94.7	0.602	0.418 to 0.765	4.42	2.63 to 7.66

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale < 14 (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Stein 1995[139]	751	18.1	94.1	19.4	12.4 to 27.9	94.2	92.2 to 95.8	0.856	0.765 to 0.933	3.33	1.95 to 5.41
Mandera 2000[133]	166	22.1	85.7	24.0	15.0 to 34.8	86.6	79.0 to 92.3	0.879	0.746 to 1.014	1.78	0.94 to 3.43
Dunning 2006[30]	22,772	45.9	99.4	45.1	39.3 to 51.0	99.4	99.3 to 99.5	0.552	0.493 to 0.611	73.48	59.56 to 91.00
Atabaki 2008[81]	1000	90.8	2.7	89.7	80.7 to 95.6	2.7	1.8 to 3.8	3.858	1.534 to 8.154	0.92	0.83 to 0.98
Guzel 2009[87]	337	20.9	98.5	21.1	12.9 to 31.3	98.6	96.8 to 99.6	0.802	0.697 to 0.885	14.90	5.78 to 48.58
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	< 0.001	< 0.001	40.4	12.8 to 77.5	89.1	18.9 to 99.6	0.718	0.429 to 1.674	3.58	0.80 to 46.84

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Focal neurological deficit (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Chan 1990[212]	418	7.7	96.0	33.8	9.9 to 45.7	96.6	94.6 to 98.1	0.683	0.568 to 0.935	10.07	2.63 to 16.23
Dietrich 1993[84]	252	28.6	94.5	37.8	21.2 to 49.3	95.6	92.4 to 97.6	0.648	0.538 to 0.831	8.75	3.69 to 14.70
Ramundo 1995[135]	261	11.1	99.5	12.1	5.4 to 21.5	99.7	98.8 to 99.9	0.883	0.791 to 0.948	36.64	9.68 to 112.20
Quayle 1997[94]	321	40.7	85.0	56.6	32.3 to 67.4	86.1	81.8 to 89.7	0.500	0.384 to 0.793	4.03	2.14 to 5.55
Ng 2002[134]	119	12.3	100.0	12.1	5.9 to 20.6	99.7	98.4 to 100.0	0.883	0.800 to 0.943	39.00	8.33 to 148.00
Da Dalt 2006[83]	3796	25.0	99.8	12.2	6.7 to 25.9	99.8	99.6 to 99.9	0.880	0.743 to 0.935	48.31	26.62 to 125.20
Dunning 2006[30]	22,772	19.2	99.6	16.9	12.9 to 22.0	99.6	99.5 to 99.6	0.835	0.783 to 0.874	38.00	27.43 to 54.56
Oman 2006[91]	1666	81.0	68.0	76.9	69.2 to 84.4	67.8	65.5 to 70.2	0.340	0.230 to 0.456	2.39	2.11 to 2.70
Atabaki 2008[81]	1000	3.1	99.6	8.1	2.8 to 15.0	99.8	99.3 to 99.9	0.921	0.854 to 0.975	41.38	6.97 to 102.6
Guzel 2009[87]	337	3.0	100.0	3.8	1.0 to 9.5	100.0	99.7 to 100.0	0.962	0.907 to 0.990	87.38	12.21 to 503.50

continued

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	10	<0.001	<0.001	21.1	8.8 to 41.1	99.0	95.4 to 99.8	0.798	0.615 to 0.915	20.46	7.40 to 54.24

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Depressed skull fracture (intracranial injury – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	261	26.7	96.8	26.7	15.8 to 41.3	96.8	93.4 to 98.4	0.758	0.467 to 1.231	8.23	3.43 to 19.74
Dunning 2006[30]	22,772	13.9	99.9	13.9	10.3 to 18.4	99.9	99.9 to 99.9	0.862	0.759 to 0.978	173.42	100.4 to 299.3

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.032	<0.001	16.0	12.4 to 20.5	99.8	99.7 to 99.9	0.855	0.756 to 0.966	73.82	46.45 to 117.32

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Basal skull fracture (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Reed 2005[136]	39	30.0	93.1	28.1	11.6 to 49.9	96.6	90.0 to 99.3	0.744	0.535 to 0.913	11.12	2.53 to 24.08
Da Dalt 2006[83]	3806	9.1	99.8	8.7	3.1 to 18.3	99.7	99.6 to 99.9	0.916	0.820 to 0.972	35.58	12.71 to 88.00
Dunning 2006[30]	22,772	30.2	98.0	27.5	21.9 to 33.6	98.0	97.8 to 98.2	0.740	0.678 to 0.797	13.64	10.65 to 17.01
Atabaki 2008[81]	1000	4.6	97.6	17.2	4.7 to 26.4	98.3	97.1 to 99.1	0.843	0.751 to 0.975	11.07	2.10 to 18.86
Kupperman 2009[90]	31,396	13.5	99.4	13.4	9.7 to 17.5	99.4	99.3 to 99.5	0.872	0.831 to 0.909	21.53	15.26 to 29.07

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	< 0.001	< 0.001	17.8	7.8 to 31.7	98.7	96.5 to 99.6	0.833	0.703 to 0.929	16.90	6.13 to 32.44

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any seizure (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dietrich 1993[84]	253	11.1	94.5	10.0	7.0 to 13.7	94.8	91.4 to 97.1	0.949	0.907 to 0.999	1.92	1.02 to 3.70
Ramundo 1995[135]	256	11.9	95.8	10.0	7.3 to 13.3	96.0	93.0 to 98.0	0.937	0.900 to 0.981	2.51	1.29 to 5.21
Schunk 1996[137]	313	7.7	92.0	10.0	6.7 to 14.3	92.3	89.0 to 95.0	0.975	0.924 to 1.028	1.31	0.74 to 2.22
Fridriksson 2000[130]	49	22.7	88.9	10.0	6.8 to 14.7	92.4	80.2 to 97.8	0.973	0.909 to 1.120	1.33	0.47 to 4.69
Ng 2002[134]	119	6.2	88.9	9.9	6.5 to 14.3	91.1	82.2 to 96.4	0.987	0.918 to 1.107	1.13	0.47 to 2.97
Reed 2005[136]	39	20.0	96.6	10.1	7.3 to 13.6	96.7	89.0 to 99.4	0.931	0.889 to 1.014	3.07	0.88 to 16.95
Dunning 2006[30]	22,772	10.0	99.6	10.1	7.2 to 13.8	99.6	99.5 to 99.7	0.902	0.866 to 0.932	27.40	18.36 to 40.06
Atabaki 2008[81]	1000	10.8	94.7	10.0	7.0 to 13.6	94.7	93.2 to 96.0	0.950	0.911 to 0.985	1.90	1.22 to 2.85
Guzel 2009[87]	337	7.5	98.1	10.0	7.6 to 12.8	98.0	96.0 to 99.2	0.919	0.888 to 0.950	5.05	2.36 to 12.58
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	9	0.602	< 0.001	10.0	7.3 to 13.3	96.3	91.9 to 98.3	0.935	0.899 to 0.987	2.69	1.17 to 6.24

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any loss of consciousness (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Chan 1990[212]	418	61.5	67.4	56.2	36.4 to 75.3	67.5	62.9 to 72.0	0.650	0.366 to 0.950	1.73	1.10 to 2.4
Dietrich 1993[84]	179	67.9	60.3	63.2	47.3 to 77.7	60.6	52.6 to 68.1	0.608	0.366 to 0.893	1.60	1.14 to 2.2
Davis 1994[129]	138	60.0	68.8	54.6	33.3 to 75.3	69.1	60.8 to 76.5	0.659	0.356 to 0.982	1.76	1.04 to 2.7
Ramundo 1995[135]	212	70.6	59.0	65.9	51.3 to 79.1	59.2	51.9 to 66.2	0.577	0.351 to 0.839	1.61	1.21 to 2.10
Schunk 1996[137]	313	15.5	73.7	30.9	13.5 to 50.8	74.0	68.9 to 78.7	0.935	0.663 to 1.181	1.19	0.51 to 2.0
Fridriksson 2000[130]	49	45.5	66.7	46.9	30.1 to 64.0	69.0	51.3 to 83.3	0.774	0.508 to 1.130	1.50	0.83 to 3.0
Simon 2001[138]	429	38.7	52.9	41.1	30.0 to 52.8	53.3	48.1 to 58.3	1.106	0.873 to 1.351	0.88	0.63 to 1.2
Ng 2002[134]	119	47.7	61.1	48.3	37.2 to 59.5	62.7	49.8 to 74.4	0.826	0.618 to 1.108	1.29	0.88 to 2.0
Reed 2005[136]	39	50.0	86.2	46.3	25.8 to 68.5	85.5	71.5 to 94.4	0.632	0.372 to 0.890	3.17	1.40 to 8.46
Boran 2006[128]	421	37.8	97.7	36.3	23.5 to 51.0	97.3	95.4 to 98.6	0.655	0.505 to 0.787	13.35	6.81 to 27.5
Da Dalt 2006[83]	3793	38.1	97.4	35.9	20.6 to 54.1	97.3	96.8 to 97.8	0.659	0.472 to 0.816	13.44	7.56 to 21.3
Dunning 2006[30]	22,772	51.2	95.4	50.6	44.8 to 56.3	95.4	95.1 to 95.6	0.519	0.458 to 0.579	10.91	9.56 to 12.4
Oman 2006[91]	1666	75.0	45.0	73.3	65.8 to 80.0	45.1	42.6 to 47.6	0.592	0.441 to 0.764	1.33	1.19 to 1.5
Atabaki 2008[81]	1000	23.1	66.7	27.4	17.8 to 38.4	66.9	63.8 to 69.9	1.086	0.916 to 1.240	0.83	0.53 to 1.2
Guzel 2009[87]	337	13.4	93.7	17.6	9.9 to 27.3	93.8	90.5 to 96.2	0.879	0.775 to 0.967	2.81	1.40 to 5.4
Klemetti 2009[89]	485	53.0	68.7	51.4	41.2 to 61.6	91.1	87.7 to 94.0	0.534	0.421 to 0.647	5.79	3.93 to 8.8
Kupperman 2009[90]	28,195	36.6	87.6	37.0	30.1 to 44.4	87.6	87.2 to 88.0	0.719	0.635 to 0.798	2.98	2.42 to 3.58
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	17	< 0.001	< 0.001	45.9	36.4 to 55.6	80.1	67.4 to 87.3	0.679	0.566 to 0.814	2.30	1.46 to 3.47

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any headache (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Chan 1990[212]	418	15.4	75.6	25.8	12.5 to 41.8	75.9	71.6 to 79.9	0.978	0.772 to 1.159	1.07	0.52 to 1.73
Dietrich 1993[84]	194	50.0	51.7	52.7	34.7 to 69.6	52.7	45.6 to 59.7	0.898	0.584 to 1.259	1.11	0.73 to 1.49
Davis 1994[129]	168	33.3	77.6	30.4	16.4 to 48.9	77.3	70.6 to 83.2	0.901	0.671 to 1.080	1.34	0.74 to 2.21
Ramundo 1995[135]	185	66.7	32.9	69.6	49.6 to 84.6	34.4	27.7 to 41.6	0.881	0.455 to 1.507	1.06	0.76 to 1.31
Schunk 1996[137]	313	38.4	70.3	37.3	22.0 to 55.1	70.4	65.2 to 75.3	0.890	0.641 to 1.109	1.26	0.75 to 1.88
Fridriksson 2000[130]	49	40.9	66.7	40.1	24.8 to 57.0	67.8	52.7 to 80.5	0.886	0.655 to 1.153	1.24	0.77 to 2.0
Ng 2002[134]	119	12.3	85.2	14.6	8.1 to 23.2	86.2	77.5 to 92.5	0.990	0.891 to 1.107	1.06	0.55 to 1.98
Haydel 2003[88]	175	50.0	66.5	44.5	27.9 to 62.8	66.3	59.1 to 73.0	0.838	0.568 to 1.089	1.32	0.84 to 1.91
Reed 2005[136]	39	10.0	100.0	9.7	2.1 to 26.0	93.5	84.1 to 98.4	0.970	0.822 to 1.046	1.45	0.51 to 4.77
Da Dalt 2006[83]	3800	25.0	91.1	16.4	7.6 to 32.0	91.0	90.1 to 91.9	0.918	0.748 to 1.015	1.83	0.85 to 3.60
Dunning 2006[30]	22,772	20.3	79.0	21.0	16.6 to 25.9	79.0	78.5 to 79.5	1.000	0.938 to 1.056	1.00	0.79 to 1.23
Atabaki 2008[81]	1000	26.2	61.7	31.4	21.2 to 42.8	62.2	59.0 to 65.2	1.103	0.916 to 1.282	0.83	0.55 to 1.14
Guzel 2009[87]	337	32.8	83.7	29.7	20.7 to 40.5	82.8	78.2 to 86.9	0.850	0.717 to 0.966	1.72	1.15 to 2.57
Kupperman 2009[90]	27,495	73.4	54.1	71.3	64.9 to 77.1	54.1	53.5 to 54.7	0.531	0.424 to 0.648	1.55	1.41 to 1.68
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	14	< 0.001	< 0.001	33.9	22.9 to 47.6	73.3	62.1 to 81.3	0.905	0.784 to 1.010	1.26	0.97 to 1.61

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Anterograde or post-trauma amnesia (intracranial injury – children)

Study	Observed estimates		Fixed-effects estimates[a]							
	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Guzel 2009[87]	20.9	93.0	20.9	12.8 to 32.3	93.0	89.2 to 95.5	0.851	0.401 to 1.804	2.97	1.40 to 6.29

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Undefined vomiting (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Chan 1990[212]	418	38.5	73.8	34.7	18.2 to 55.4	73.9	69.5 to 78.0	0.883	0.603 to 1.117	1.33	0.69 to 2.19
Dietrich 1993[84]	253	27.8	59.4	28.9	17.3 to 43.0	60.2	53.7 to 66.3	1.181	0.932 to 1.431	0.73	0.42 to 1.11
Davis 1994[129]	168	8.3	93.6	18.8	5.7 to 38.2	92.4	87.7 to 95.8	0.880	0.669 to 1.027	2.46	0.72 to 6.14
Ramundo 1995[135]	218	13.9	79.7	18.7	9.0 to 31.2	79.7	73.6 to 85.0	1.021	0.856 to 1.172	0.92	0.43 to 1.65
Schunk 1996[137]	313	46.1	65.7	39.3	21.6 to 60.9	66.0	60.6 to 71.1	0.920	0.590 to 1.206	1.16	0.62 to 1.84
Fridriksson 2000[130]	49	63.6	66.7	52.6	35.2 to 71.2	68.4	51.0 to 82.4	0.696	0.411 to 1.050	1.66	0.93 to 3.2
Ng 2002[134]	119	41.5	50.0	40.2	29.4 to 51.7	53.2	40.4 to 65.6	1.122	0.834 to 1.542	0.86	0.58 to 1.28
Haydel 2003[88]	175	42.9	82.6	36.5	19.9 to 57.4	82.3	76.1 to 87.5	0.773	0.516 to 0.987	2.05	1.05 to 3.64
Reed 2005[136]	39	0.0	72.4	18.2	5.1 to 36.9	74.3	58.2 to 86.6	1.099	0.825 to 1.457	0.71	0.19 to 1.79
Da Dalt 2006[83]	3803	23.8	87.1	25.8	12.8 to 42.4	87.1	86.0 to 88.2	0.852	0.661 to 1.002	2.00	0.99 to 3.32
Dunning 2006[30]	22,772	40.9	89.4	40.3	34.7 to 46.1	89.4	89.0 to 89.8	0.668	0.603 to 0.731	3.80	3.26 to 4.38
Atabaki 2008[81]	1000	26.2	66.3	27.1	17.9 to 37.8	66.4	63.4 to 69.4	1.098	0.932 to 1.248	0.81	0.53 to 1.14
Guzel 2009[87]	337	25.4	54.8	26.7	17.6 to 37.1	55.5	49.6 to 61.3	1.321	1.101 to 1.557	0.60	0.39 to 0.86
Kupperman 2009[90]	31,476	35.5	87.5	35.2	29.8 to 40.9	87.5	87.1 to 87.9	0.740	0.676 to 0.803	2.82	2.38 to 3.28
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	14	<0.001	<0.001	30.9	21.6 to 40.1	76.0	68.1 to 83.8	0.910	0.774 to 1.059	1.29	0.85 to 1.99

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined or mixed amnesia (intracranial injury – children)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dietrich 1993[84]	159	87.1	45.3	77.7	54.5 to 90.9	44.9	36.4 to 53.5	0.497	0.201 to 1.059	1.41	0.96 to 1.78
Ramundo 1995[135]	178	56.3	49.4	54.3	34.9 to 74.3	49.9	42.3 to 57.5	0.915	0.512 to 1.346	1.08	0.69 to 1.53
Schunk 1996[137]	313	22.9	80.3	28.8	12.2 to 48.3	80.6	75.9 to 84.8	0.884	0.643 to 1.097	1.48	0.62 to 2.58

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Fridriksson 2000[130]	49	31.8	74.1	33.8	18.7 to 51.0	76.3	59.8 to 88.5	0.869	0.638 to 1.165	1.42	0.68 to 3.01
Ng 2002[134]	119	15.4	87.0	17.9	10.0 to 28.6	88.5	78.9 to 94.8	0.929	0.794 to 1.072	1.56	0.68 to 3.82
Reed 2005[136]	39	20.0	100.0	17.2	4.6 to 38.9	96.7	88.2 to 99.6	0.863	0.643 to 0.987	5.05	1.22 to 39.56
Dunning 2006[30]	22,772	24.6	97.1	23.8	19.0 to 29.0	97.1	96.9 to 97.3	0.785	0.731 to 0.835	8.20	6.46 to 10.16
Atabaki 2008[81]	1000	23.1	67.8	26.5	16.6 to 39.5	68.0	65.0 to 71.0	1.081	0.886 to 1.236	0.83	0.52 to 1.25
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	8	<0.001	<0.001	33.4	17.8 to 52.4	81.4	63.1 to 93.3	0.821	0.642 to 0.998	1.82	1.00 to 3.74

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Severe or persistent headache (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Reed 2005[136]	39	0.0	75.9	20.4	13.8 to 29.2	80.6	64.8 to 92.2	0.994	0.876 to 1.206	1.17	0.58 to 2.19
Da Dalt 2006[83]	3800	25.0	98.1	11.1	8.5 to 14.0	98.1	97.6 to 98.5	0.907	0.878 to 0.933	5.80	4.27 to 7.73
Dunning 2006[30]	22,772	6.0	99.7	7.0	4.5 to 10.0	99.7	99.6 to 99.7	0.933	0.904 to 0.958	20.26	12.56 to 30.44
Oman 2006[91]	1666	20.0	85.0	19.3	13.9 to 25.4	85.0	83.2 to 86.8	0.949	0.876 to 1.016	1.29	0.92 to 1.74
Kupperman 2009[90]	26,494	12.7	97.0	12.4	9.8 to 15.3	97.0	96.8 to 97.2	0.903	0.873 to 0.929	4.19	3.29 to 5.20
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	<0.001	<0.001	13.5	7.8 to 21.5	94.9	81.8 to 99.3	0.916	0.872 to 0.986	4.35	1.07 to 12.35

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Radiological skull fracture (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Chan 1990[212]	418	100.0	96.8	43.9	38.5 to 51.5	96.5	94.4 to 98.0	0.583	0.506 to 0.635	12.43	8.03 to 21.53
Quayle 1997[94]	321	51.9	87.8	49.0	43.2 to 55.5	87.8	83.8 to 91.3	0.581	0.509 to 0.649	4.04	3.01 to 5.57
Mandera 2000[133]	166	51.7	32.1	59.5	49.9 to 68.8	33.7	25.2 to 43.0	1.199	0.849 to 1.725	0.90	0.73 to 1.10
Wang 2000[140]	157	46.7	88.2	48.7	42.7 to 55.1	88.5	82.3 to 93.2	0.581	0.512 to 0.652	4.24	2.79 to 6.90
Boran 2006[128]	421	43.2	93.0	46.4	41.0 to 52.2	93.1	90.2 to 95.3	0.577	0.517 to 0.634	6.67	4.77 to 9.7
Dunning 2006[30]	22,772	34.9	99.3	37.0	31.7 to 42.4	99.3	99.2 to 99.4	0.635	0.581 to 0.688	51.58	41.74 to 63.64
Keskil 1995[132]	257	70.0	61.2	55.4	47.5 to 64.2	61.2	54.8 to 67.4	0.728	0.580 to 0.879	1.43	1.16 to 1.77
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	7	<0.001	<0.001	48.4	40.8 to 57.3	89.3	67.7 to 97.3	0.585	0.516 to 0.708	4.55	1.64 to 15.73

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Post-trauma seizure (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Davis 1994[129]	168	8.3	96.2	6.9	3.4 to 11.5	96.6	93.4 to 98.6	0.965	0.904 to 1.023	2.49	0.64 to 7.08
Haydel 2003[88]	175	0.0	96.3	6.7	3.3 to 11.2	96.4	93.2 to 98.6	0.968	0.908 to 1.026	2.32	0.60 to 6.51
Boran 2006[128]	421	13.5	99.7	13.5	6.4 to 23.3	99.4	98.6 to 99.9	0.870	0.770 to 0.943	39.81	6.41 to 164.30
Da Dalt 2006[83]	3803	13.6	99.4	12.9	6.3 to 22.3	99.4	99.2 to 99.6	0.876	0.781 to 0.943	23.20	9.59 to 47.78
Oman 2006[91]	1666	6.0	94.0	5.4	2.7 to 9.1	94.1	92.9 to 95.2	1.006	0.965 to 1.038	0.92	0.45 to 1.61
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	0.493	0.810	8.7	4.2 to 15.7	98.0	94.5 to 99.6	0.932	0.849 to 1.004	8.49	0.93 to 31.66

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Scalp laceration (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Davis 1994[129]	168	41.7	84.0	12.3	3.8 to 56.2	86.4	79.4 to 90.7	1.001	0.521 to 1.114	0.99	0.31 to 3.85
Reed 2005[136]	39	0.0	96.6	5.7	0.0 to 14.9	90.6	86.0 to 97.5	1.045	0.946 to 1.108	0.54	0.00 to 1.58
Atabaki 2008[81]	1000	3.1	89.7	6.0	1.1 to 13.5	89.5	87.5 to 91.4	1.050	0.966 to 1.107	0.57	0.11 to 1.31
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.002	0.051	7.4	0.1 to 33.7	89.1	83.0 to 94.7	1.040	0.782 to 1.107	0.67	0.02 to 2.27

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Scalp haematoma (intracranial injury – children)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Davis 1994[129]	168	25.0	84.0	33.6	15.6 to 52.3	81.7	75.4 to 87.4	0.813	0.591 to 1.017	1.86	0.92 to 3.07
Reed 2005[136]	39	20.0	72.4	41.3	21.1 to 56.4	75.6	64.7 to 85.3	0.775	0.618 to 0.968	1.71	1.12 to 2.46
Oman 2006[91]	1666	59.0	63.0	57.6	49.7 to 65.3	63.3	60.8 to 65.7	0.670	0.548 to 0.796	1.57	1.34 to 1.80
Atabaki 2008[81]	1000	43.1	73.5	45.2	35.5 to 54.2	73.5	70.7 to 76.2	0.747	0.625 to 0.875	1.71	1.34 to 2.08
Guzel 2009[87]	337	56.7	68.9	52.2	44.4 to 60.2	68.4	63.5 to 73.2	0.699	0.596 to 0.799	1.66	1.41 to 1.94
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	5	<0.001	<0.001	45.4	27.0 to 57.6	73.1	64.9 to 82.5	0.745	0.615 to 0.918	1.70	1.30 to 2.23

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Need for neurosurgery in children

Glasgow Coma Scale <15 (neurosurgery – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Hahn 1993[131]	791	41.8	70.4	41.8	30.6 to 53.8	70.4	67.0 to 73.7	0.826	0.597 to 1.144	1.41	0.95 to 2.10
Stein 1995[139]	751	54.2	78.5	54.2	34.6 to 72.5	78.5	75.4 to 81.4	0.584	0.321 to 1.060	2.52	1.43 to 4.44
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.298	<0.001	45.1	35.1 to 55.4	74.3	72.0 to 76.5	0.763	0.573 to 1.015	1.71	1.24 to 2.36

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Glasgow Coma Scale <14 (neurosurgery – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Hahn 1993[131]	791	23.9	85.9	23.9	15.2 to 35.5	85.9	83.2 to 88.3	0.886	0.666 to 1.179	1.70	1.00 to 2.87
Stein 1995[139]	751	25.0	93.1	25.0	11.7 to 45.6	93.1	91.0 to 94.7	0.805	0.504 to 1.286	3.64	1.56 to 8.48
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.912	<0.001	24.2	16.5 to 34.0	88.9	87.2 to 90.5	0.863	0.677 to 1.102	2.10	1.34 to 3.28

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any seizure (neurosurgery – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schunk 1996[137]	33.3	92.3	33.3	4.3 to 84.6	92.3	88.7 to 94.8	0.723	0.324 to 1.610	4.31	0.83 to 22.33

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Post-trauma seizure (neurosurgery – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Haydel 2003[88]	0.0	96.3	8.3	0.5 to 62.2	96.3	92.0 to 98.3	0.952	0.924 to 0.982	0.09	0.01 to 1.38

a Assumes normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Any loss of consciousness (neurosurgery – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schunk 1996[137]	0.0	73.9	16.7	1.0 to 80.6	73.9	68.7 to 78.5	1.128	0.054 to 23.748	0.64	0.03 to 13.43

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Any headache (neurosurgery – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schunk 1996[137]	313	33.3	70.0	33.3	4.3 to 84.6	70.0	64.7 to 74.8	0.952	0.192 to 4.727	1.11	0.22 to 5.56
Haydel 2003[88]	175	83.3	66.9	83.3	36.9 to 97.7	66.9	59.4 to 73.5	0.249	0.172 to 0.362	2.51	1.66 to 3.82
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.161	0.479	64.2	26.6 to 89.9	68.9	64.6 to 72.9	0.267	0.186 to 0.384	2.39	1.60 to 3.58

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined vomiting (neurosurgery – children)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schunk 1996[137]	313	66.7	65.5	66.7	15.4 to 95.7	65.5	60.0 to 70.6	0.509	0.228 to 1.138	1.93	0.48 to 7.82
Haydel 2003[88]	175	50.0	81.7	50.0	16.8 to 83.2	81.7	75.1 to 86.8	0.612	0.274 to 1.367	2.73	0.83 to 8.92

continued

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.638	< 0.001	55.3	24.6 to 82.4	70.4	66.1 to 74.4	0.558	0.316 to 0.986	2.36	0.96 to 5.83

a Assuming normal distribution on the logarithm scale
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined or mixed amnesia (neurosurgery – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Schunk 1996[137]	0.0	80.0	16.7	1.0 to 80.6	80.0	75.2 to 84.1	1.042	0.049 to 21.976	0.83	0.04 to 17.58

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Radiological skull fracture (neurosurgery – children)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Hahn 1993[131]	73.1	53.3	73.1	61.3 to 82.4	53.3	49.7 to 56.9	0.504	0.337 to 0.752	1.57	1.33 to 1.85

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Intracranial injury in infants

Fall – any (intracranial injury – infants)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	37	62.5	20.7	62.5	28.5 to 87.5	20.7	9.6 to 39.0	1.813	0.743 to 4.423	0.79	0.45 to 1.39
Buchanich 2007[82]	97	68.2	25.3	68.2	46.6 to 84.0	25.3	16.8 to 36.3	1.256	0.776 to 2.034	0.91	0.67 to 1.25

		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.771	0.620	66.6	48.3 to 81.0	24.1	16.8 to 33.3	1.365	0.893 to 2.085	0.88	0.67 to 1.16

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Coagulopathy (intracranial injury – infants)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Oman 2006[91]	4.0	97.0	4.0	0.6 to 23.5	97.0	94.2 to 98.5	0.990	0.911 to 1.075	1.33	0.17 to 10.16

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Motor vehicle collision – in car (intracranial injury – infants)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	25.0	93.1	25.0	6.3 to 62.3	93.1	76.2 to 98.3	0.806	0.533 to 1.216	3.63	0.60 to 21.86

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Persistent vomiting (intracranial injury – infants)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Oman 2006[91]	13.0	87.0	13.0	4.5 to 32.4	87.0	82.6 to 90.4	1.000	0.296 to 3.373	1.00	0.30 to 3.37

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Glasgow Coma Scale <15 (intracranial injury – infants)

Study	*n*	Observed estimates		Posterior median estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	37	50.0	82.8	52.0	38.0 to 68.7	84.0	69.2 to 93.2	0.574	0.404 to 0.719	3.30	1.82 to 6.33
Oman 2006[91]	309	72.0	58.1	67.9	49.0 to 84.3	58.4	52.6 to 64.0	0.551	0.268 to 0.885	1.63	1.15 to 2.13
Kupperman 2009[90]	10,718	33.7	96.0	34.6	25.5 to 44.3	96.0	95.6 to 96.4	0.682	0.580 to 0.776	8.62	6.29 to 11.24
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	3	0.004	< 0.001	51.9	34.4 to 75.8	84.5	45.8 to 95.2	0.586	0.377 to 0.791	3.38	1.24 to 8.02

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Focal neurological deficit (intracranial injury – infants)

Study	Observed estimates		Fixed-effects estimates[a]							
	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dietrich 1993[84]	33.3	97.1	33.3	4.3 to 84.6	97.1	89.0 to 99.3	0.687	0.043 to 11.098	11.33	0.70 to 183.11

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Radiological skull fracture (intracranial injury – infants)

Study	*n*	Observed estimates		Fixed-effects estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Greenes 2001[86]	422	100.0	92.2	96.2	59.7 to 99.8	92.2	89.1 to 94.4	0.042	0.037 to 0.047	12.29	8.66 to 17.44
Buchanich 2007[82]	97	59.1	48.0	59.1	38.2 to 77.2	48.0	37.0 to 59.2	0.852	0.560 to 1.297	1.14	0.75 to 1.71
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.058	< 0.001	64.7	44.8 to 80.5	81.4	76.8 to 85.3	0.051	0.046 to 0.057	4.51	3.45 to 5.88

a Assuming normal distribution on the logarithm scale
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Depressed skull fracture (intracranial injury – infants)

	Observed estimates		Fixed-effects estimates[a]							
Study	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Ramundo 1995[135]	25.0	100.0	25.0	6.3 to 62.3	98.3	78.0 to 99.9	0.763	0.510 to 1.142	14.50	0.72 to 290.82

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

Any seizure (intracranial injury – infants)

		Observed estimates		Fixed-effects estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dietrich 1993[84]	71	0.0	100.0	16.7	1.0 to 80.6	100.0	89.3 to 100.0	1.000	0.080 to 12.564	22.67	0.54 to 959.56
Ramundo 1995[135]	37	12.5	79.3	12.5	1.7 to 53.7	79.3	61.0 to 90.4	1.103	0.175 to 6.966	0.60	0.08 to 4.32
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.858	0.017	13.7	2.8 to 47.2	84.3	69.5 to 92.7	1.066	0.240 to 4.730	1.32	0.23 to 7.55

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Any loss of consciousness (intracranial injury – infants)

		Observed estimates		Posterior median estimates[a]							
Study	*n*	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dietrich 1993[84]	58	50.0	83.9	37.8	25.4 to 54.1	84.1	73.3 to 92.0	0.741	0.576 to 0.873	2.41	1.47 to 4.07
Ramundo 1995[135]	31	16.7	64.0	47.1	31.9 to 65.3	69.7	49.7 to 85.0	0.759	0.519 to 1.075	1.57	0.90 to 2.85
Oman 2006[91]	309	64.0	68.0	49.1	34.0 to 67.5	67.6	62.0 to 72.9	0.754	0.480 to 0.986	1.52	1.03 to 2.17
Kupperman 2009[90]	10,215	19.5	96.4	21.9	13.6 to 31.4	96.4	96.1 to 96.8	0.810	0.711 to 0.896	6.15	3.77 to 8.92
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	4	< 0.001	< 0.001	39.4	20.6 to 65.2	84.1	56.2 to 95.5	0.730	0.519 to 0.901	2.51	1.23 to 5.28

a Of posterior distribution for Bayesian meta-analyses.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Undefined vomiting (intracranial injury – infants)

Study	*n*	Observed estimates		Fixed-effects estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Dietrich 1993[84]	71	0.0	79.4	16.7	1.0 to 80.6	79.4	68.2 to 87.4	1.259	0.394 to 4.027	0.81	0.05 to 13.59
Ramundo 1995[135]	37	12.5	79.3	12.5	1.7 to 53.7	79.3	61.0 to 90.4	1.103	0.473 to 2.571	0.60	0.07 to 5.02
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.858	0.991	13.7	2.8 to 47.2	79.4	70.2 to 86.3	1.155	0.583 to 2.289	0.67	0.12 to 3.65

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Post-trauma seizure (intracranial injury – infants)

Study	Observed estimates		Fixed-effects estimates[a]							
	Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Oman 2006[91]	8.0	91.0	8.0	2.0 to 26.9	91.0	87.1 to 93.8	1.011	0.896 to 1.141	0.89	0.22 to 3.53

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.

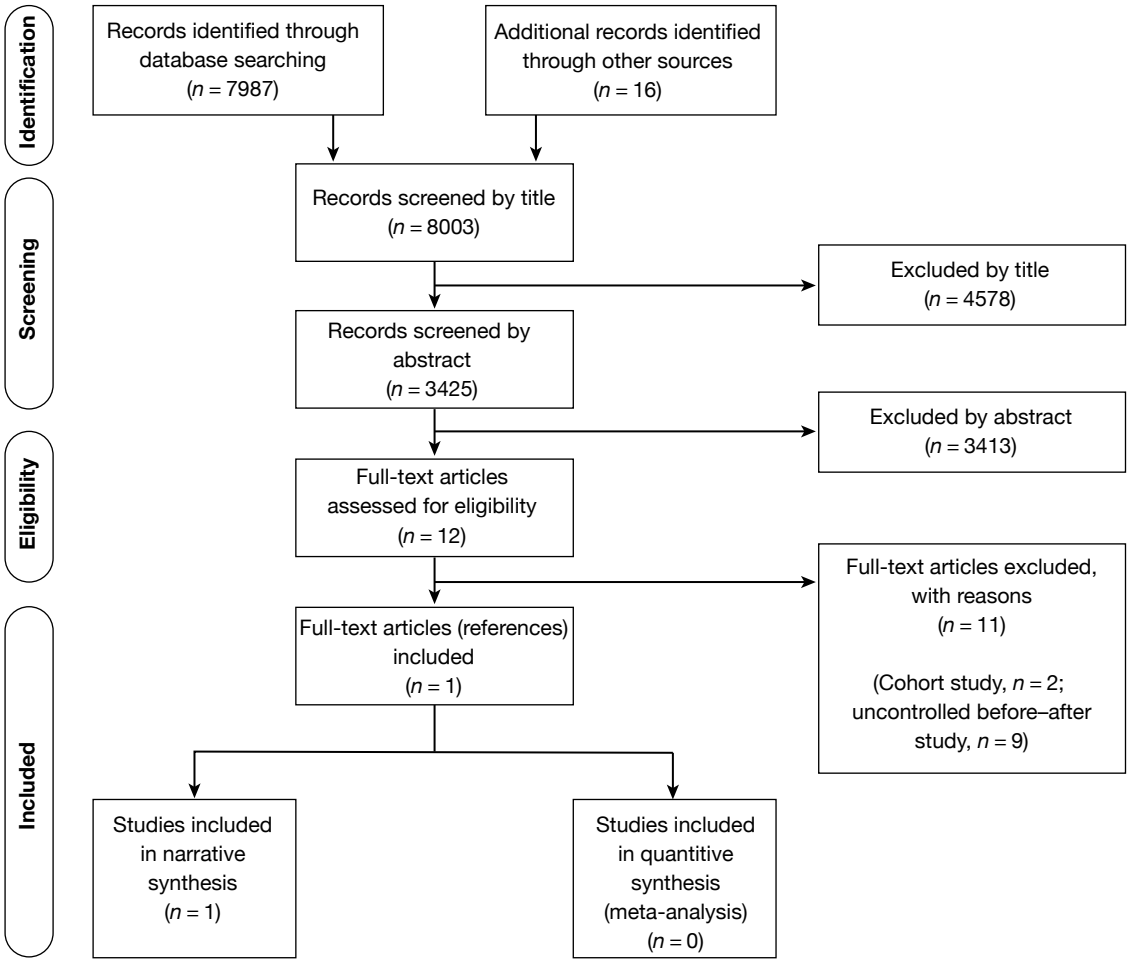
Scalp haematoma (intracranial injury – infants)

Study	*n*	Observed estimates		Fixed-effects estimates[a]							
		Sensitivity[b]	Specificity[b]	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
Oman 2006[91]	309	65.0	59.0	65.0	44.9 to 80.9	59.0	53.2 to 64.6	0.593	0.438 to 0.804	1.59	1.15 to 2.18
Kupperman 2009[90]	10,659	66.0	56.0	66.0	56.0 to 74.7	56.0	55.0 to 56.9	0.608	0.526 to 0.702	1.50	1.30 to 1.73
		Heterogeneity test *p*-value[c]		Pooled estimates							
	No. of studies	Sensitivity	Specificity	Sensitivity	95% HDR	Specificity	95% HDR	NLR	95% HDR	PLR	95% HDR
	2	0.927	0.312	65.8	56.9 to 73.6	56.1	55.1 to 57.0	0.605	0.531 to 0.689	1.51	1.33 to 1.73

a Assuming normal distribution on the logarithm scale.
b Sensitivity and specificity estimates calculated from the observed data.
c Based on *Q*-statistic.

Appendix 7

Management practices review – PRISMA (adapted) flow chart



Appendix 8

Management practices review – table of excluded studies with rationale

Author, year	Reason for exclusion
Brown *et al.* 1994[152]	Cohort study
Fabbri *et al.* 2004[153]	Cohort study
Browning *et al.* 2005[154]	Before–after study without concurrent control group
Fong *et al.* 2008[155]	Before–after study without concurrent control group
Hassan *et al.* 2005[22]	Before–after study without concurrent control group
Kerr *et al.* 2005[156]	Before–after study without concurrent control group
Loroni *et al.* 1996[157]	Before–after study without concurrent control group
Reed *et al.* 2005[136]	Before–after study without concurrent control group
Shravat *et al.* 2006[158]	Before–after study without concurrent control group
Sultan *et al.* 2004[21]	Before–after study without concurrent control group
Thomson *et al.* 1994[159]	Before–after study without concurrent control group

Appendix 9

Cost-effectiveness review: literature search strategies – a MEDLINE example

Database searched: Ovid MEDLINE(R) In-Process and Other Non-Indexed Citations and Ovid MEDLINE(R)

Platform or provider used: OvidSP

Date of coverage: 1950 to March 2010

Search undertaken: initial search 20 April 2009

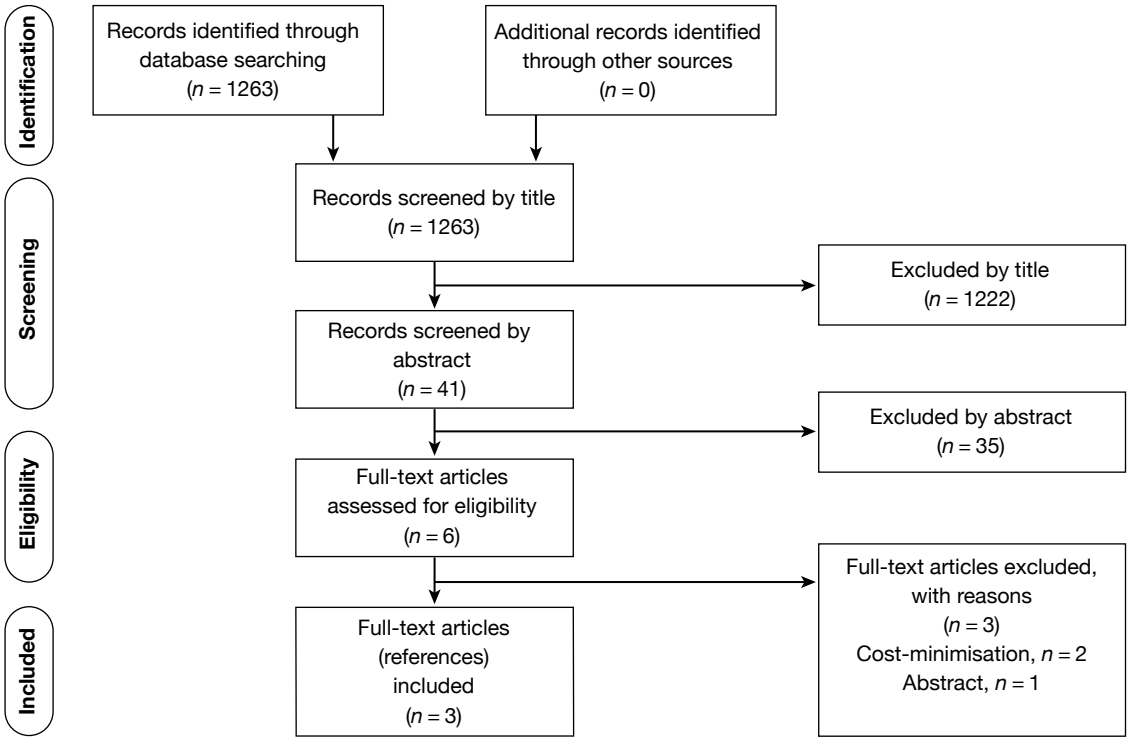
Updated search: 11 March 2010

1. *Craniocerebral Trauma/
2. head injur$.tw.
3. 1 or 2
4. Economics/
5. "costs and cost analysis"/
6. Cost allocation/
7. Cost–benefit analysis/
8. Cost control/
9. Cost savings/
10. Cost of illness/
11. 1Cost sharing/
12. "deductibles and coinsurance"/
13. Medical savings accounts/
14. Health care costs/
15. Direct service costs/
16. Drug costs/
17. Employer health costs/
18. Hospital costs/
19. Health expenditures/
20. Capital expenditures/
21. Value of life/
22. exp economics, hospital/
23. exp economics, medical/
24. Economics, nursing/
25. Economics, pharmaceutical/
26. exp "fees and charges"/
27. exp budgets/
28. (low adj cost).mp.
29. (high adj cost).mp.
30. (health?care adj cost$).mp.
31. (fiscal or funding or financial or finance).tw.
32. (cost adj estimate$).mp.

33. (cost adj variable).mp.
34. (unit adj cost$).mp.
35. (economic$or pharmacoeconomic$or price$or pricing).tw.
36. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
37. 3 and 36

Appendix 10

Cost-effectiveness review – PRISMA (adapted) flow chart



Appendix 11

Cost-effectiveness review – table of excluded studies with rationale

Author, year	Reason for exclusion
Ingebrigtsen 1996[34]	Cost-minimisation study
Burnett 2002[307]	Abstract only
Af Geijerstam 2004[35]	Cost-minimisation study

Appendix 12

Questionnaire survey (adults) sent to lead clinician

1. What guidelines, if any, do you use to assess, investigate and manage MHI in *adults*?

NICE clinical guidelines	[ ]	If NICE clinical guidelines, please clarify	
		NICE 2007	[ ]
		NICE 2003	[ ]
No guidelines	[ ]		
Other	[ ]	If 'Other', please could you enclose a copy	

2. If these are formal guidelines, have you made amendments for local use? Please *only tick yes* if you have amended the actual guidelines, not simply formatting or presentation.

Yes [ ] No [ ] If *yes*, please could you enclose a copy

3. Do you have access to a CT head scan for head injured patients (*adults*) within 4 hours at any time (24 hours per day, 7 days per week) of presentation?

Yes [ ] No [ ] If *no*, please state what restrictions apply

4a. Where are MHI patients (*adults*) admitted in hospital?

CDU	[ ]
accident and emergency observation	[ ]
formal admission	[ ]

4b. Who are they admitted under?

accident and emergency staff	[ ]
inpatient team	[ ]

4c. Who has to approve admission?

any doctor	[ ]
senior doctor	[ ]
specialist	[ ]

Appendix 13

Protocol

Project title

The cost-effectiveness of investigation and hospital admission for minor (Glasgow Coma Scale 13–15) head injury.

Planned investigation

Research objectives

We aim to identify the optimal strategy for managing adults and children with minor [Glasgow Coma Scale (GCS) 13–15] head injury. Our specific objectives are to:

- estimate the diagnostic accuracy of clinical assessment, clinical decision rules, skull radiography, cranial computerised tomography (CT) and inpatient observation for identifying intracranial bleeding requiring neurosurgery in adults and children with minor (GCS 13–15) head injury
- estimate the cost-effectiveness of diagnostic strategies for minor head injury (MHI), in terms of the cost per quality-adjusted life-year (QALY) gained by each strategy
- identify the optimal strategy for managing MHI in the NHS, defined as the most cost-effective strategy at the National Institute for Health and Clinical Excellence (NICE) threshold for willingness to pay per QALY gained
- identify the critical areas of uncertainty in the management of MHI, where future primary research would produce the most benefit.

Existing research

Head injury is responsible for around 700,000 emergency department (ED) attendances per year in England and Wales, most of which (90%) will be minor (GCS 13–15) and will not need immediate neurosurgical intervention or inpatient care.[1] These patients have a small (< 1%), but important risk of subsequent deterioration due to intracranial bleeding. If these cases are recognised and treated early then a full recovery can be expected; if not then severe disability or death may ensue.

Potential diagnostic management strategies for MHI typically use a combination of clinical assessment, skull radiography, CT scanning and hospital admission for observation to detect intracranial bleeding. The choice of strategy will have substantial cost implications for the NHS because it will be applied to hundreds of thousands of patients each year. Only a small proportion of patients will have intracranial bleeding, but those who do have a huge potential to benefit from early diagnosis and treatment.

Guidelines for managing head injury were drawn up by NICE in 2003[1] and revised in 2007.[2] These guidelines were based upon literature review and expert consensus. Cost-effectiveness analysis was not used to develop the guidelines, but was used to explore the potential impact upon health service costs. The guidelines were expected to potentially reduce costs, but recent data (outlined below) suggest that costs may have substantially increased. Additional expenditure on MHI may represent a worthwhile use of NHS resources but there are currently no relevant

analyses to support this. An extensive evidence synthesis and economic evaluation is thus needed to inform future NICE guidance.

Clinical assessment can be used to identify patients with an increased risk of intracranial bleeding and select patients for imaging or admission. A recent meta-analysis of 35 studies reporting data from 83,636 adults with head injury[3] found that severe headache (relative risk 2.44), nausea (2.16), vomiting (2.13), loss of consciousness (LOC) (2.29), amnesia (1.32), post-traumatic seizure (PTS) (3.24), old age (3.70), male gender (1.26), fall from a height (1.61), pedestrian crash victim (1.70), abnormal GCS score (5.58), focal neurology (1.80) and evidence of alcohol intake (1.62) were all associated with intracranial bleeding. A similar analysis of 16 studies reporting data from 22,420 children with head injury[4] found that focal neurology (9.43), LOC (2.23) and abnormal GCS score (5.51) were associated with intracranial bleeding.

Clinical features have been combined in a number of studies to develop a structured clinical decision rule. A systematic review undertaken for the NICE guidance[1] identified four studies of four different clinical decision rules. The studies of the Canadian CT rule[5] and the New Orleans rule[6] were both high quality, applicable to the NHS and reported 100% sensitivity for the need for neurosurgical intervention. The other two studies,[7,8] respectively, reported poor sensitivity and were not applicable to the NHS.

Several further studies have been published and new rules developed since the NICE review. A comparison of the Canadian CT and New Orleans rules undertaken by the researchers who developed the Canadian rule[9] showed that both rules had 100% sensitivity for predicting neurosurgical intervention and clinically important brain injury, but the Canadian rule had higher specificity (76.3% vs 12.1% and 50.6% vs 12.7%). A comparison by an independent team[10] found that both rules had 100% sensitivity for neurosurgical intervention, but the New Orleans rule had higher sensitivity for clinically significant brain injury (99.4% vs 87.2%), while the Canadian rule had higher specificity (39.7% vs 5.6%). This team also developed a new rule, the CT in Head Injury Patients (CHIP) rule, with 100% sensitivity and 30% specificity for neurosurgical intervention.[11]

New rules have also been developed for children with head injury. The National Emergency X-Radiography Utilization Study II (NEXUS II) rule, was developed and shown to have 98.6% sensitivity and 15.1% specificity for significant ICI,[12] whereas the Children's Head injury Algorithm for the prediction of Important Clinical Events (CHALICE) rule had 98.6% sensitivity and 86.9% specificity.[13] The striking difference in specificity may be due to the use of broader selection criteria in the CHALICE study (and thus lower prevalence). Both studies had similar positive predictive value (9.5% vs 8.6%) and negative predictive value (99.1% vs 99.9%).

Skull radiography can identify fractures that are associated with a substantially increased risk of intracranial bleeding, but cannot identify intracranial bleeding itself. Skull radiography is therefore used as a screening tool to select patient for investigation or admission, but not for definitive imaging. A meta-analysis[14] found that skull fracture detected on radiograph had a sensitivity of 38% and specificity of 95% for intracranial bleeding. More recent meta-analyses in adults[3] and children[4] reported relative risks of 4.08 and 6.13, respectively, for the association between skull fracture and intracranial bleeding.

Computerised tomography definitively shows significant bleeding and a normal CT scan effectively excludes a significant bleed at the time of scanning. MRI scanning can detect some lesions that are not evident on CT,[15] but arguably none that is of clinical importance and certainly none that influences early management. CT can therefore be considered a reference standard investigation for detecting injuries of immediate clinical importance.

Hospital admission and observation may be used to identify intracranial bleeding by monitoring the patient for neurological deterioration. Although commonly used in the past, the effectiveness of this approach has not been studied extensively and has the disadvantage that neurosurgical intervention is delayed until after patient deterioration has occurred. Hospital admission and observation are usually used selectively, based upon clinical assessment or skull radiography findings.

Theoretically, patients without intracranial bleeding on their CT scan do not require hospital admission. In practice, however, patients may be admitted for a number of reasons (1) CT scanning may identify abnormalities, such as minor cerebral contusions, which do not require neurosurgery and are of uncertain significance, but prompt hospital admission; (2) patients may be admitted pending CT scanning because they are deemed to need imaging but are unable to have imaging, either due to lack of availability or lack of ability to cooperate; and (3) patients may be admitted despite a normal CT because of concern about continuing symptoms, such as severe headache or vomiting, or with drug or alcohol intoxication.

Studies have compared CT-based strategies to skull radiography and/or admission to conclude that CT-based strategies are more likely to detect intracranial bleeding and less likely to require hospital admission.[16,17] Cost analyses based upon trial data[18] and modelling[19] both suggest that a CT-based strategy is cheaper. However, admission-based strategies may be an inappropriate comparator for cost-effectiveness analysis because they appear to be expensive and ineffective, particularly if applied unselectively.

Computerised tomography may be used unselectively (in all patients) or selectively, based upon clinical assessment or a decision rule. A strategy of CT scanning all patients would clearly be very effective, but would have a low yield of positive results and would be expensive. The more selective the use of investigations or admission the cheaper the strategy, but the higher the risk of missed pathology. Cost-effectiveness analysis is therefore necessary to determine what level of investigation represents the most efficient use of health-care resources.

A study from the USA[20] used decision analysis modelling to examine the cost-effectiveness of strategies for managing MHI and concluded that strategies involving selective CT use or CT for all, followed by discharge if negative, were cost-effective, whereas admission-based strategies were not. There was only limited exploration of uncertainty, particularly around the estimate of the effect of early versus delayed neurosurgery, and it is not clear whether the results are applicable to the NHS.

Despite the economic importance of MHI there has been little evaluation of cost-effectiveness in the NHS. Recent NICE head injury guidance was based upon the Canadian CT head rule[9] and was anticipated to lead to more CT scans being performed, but fewer skull radiographs and admissions. A cost analysis[1] suggested that the guidelines would be cost saving, by virtue of decreasing skull radiography and admissions while increasing CT scanning. Patient outcomes were not examined and the discussion cautioned that the assumption that increased CT scanning would reduce admissions might not hold in practice.

Data from a number of studies have since confirmed that more CT scans are being performed and less skull radiography is being undertaken.[21–23] However, Hospital Episode Statistics (HES) for England show that the annual number of admissions for head injury has increased from 114,769 in 2001–2 to 155,996 in 2006–7. As average length of stay has remained relatively constant, bed-days have increased from 348,032 in 2001–2 to 443,593 in 2006–7. As *Figure 1* shows, the increase in admissions has been seen in adults rather than children.[24]

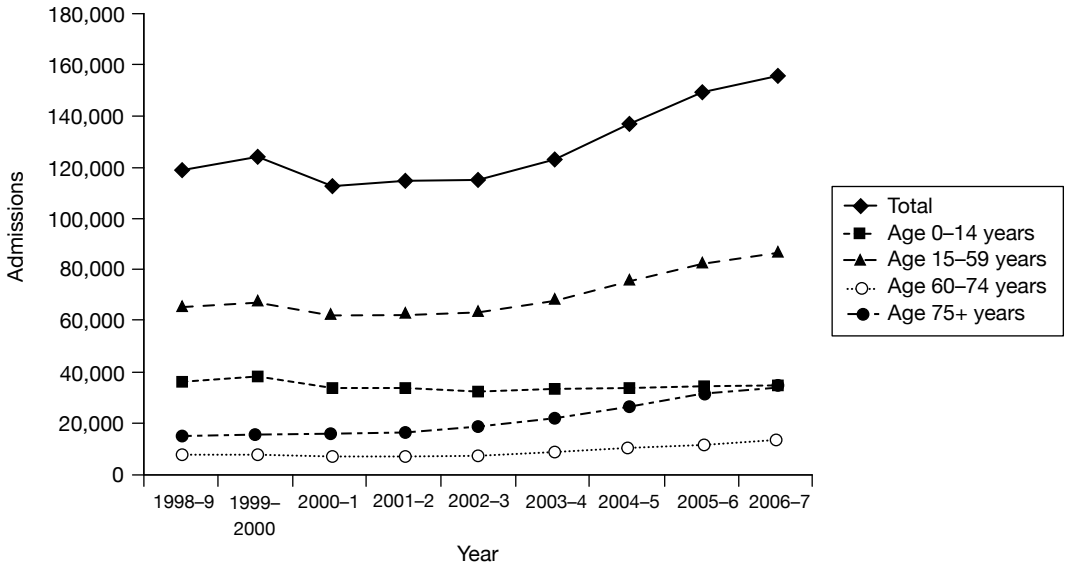


FIGURE 1 Head injury admissions in England, 1998–2007.

These data suggest that the annual costs of admission for head injury have increased from around £170M to £213M since the guidelines were introduced. Additional expenditure may be justified if associated with improved outcomes, but the anticipated effect of the guidelines was originally estimated only in resource terms and published studies have not examined effects upon patient health. It is therefore not clear whether this additional expenditure has produced any health benefits.

Management guidelines of the NHS should be based upon rigorous cost-effectiveness analysis. This is particularly important for MHI, where guideline development involves a trade-off between the costs of investigation and the benefits of detecting pathology, and where guideline implementation has substantial resource implications for the NHS.

Research methods

Design

We plan to undertake a cost-effectiveness analysis based on secondary research (systematic review, meta-analysis and decision-analysis modelling), along with a national survey and analysis of routine data sources to determine the most appropriate diagnostic management strategy for adults and children with minor head injuries in the NHS.

Systematic review and meta-analysis

Using standard methodology, we will undertake systematic literature reviews to identify:

- cohort studies of patients with head injury that measure the diagnostic accuracy of any element of clinical assessment, any clinical decision rule, skull radiography, cranial CT or observation strategy for identifying intracranial injuries that require neurosurgery
- observational or experimental studies that evaluate diagnostic management strategies for MHI in terms of process measures (hospital admissions, length of stay, time to neurosurgery) or patient outcomes
- studies that report data to estimate key parameters in the decision-analysis model: prevalence of intracranial bleeding in MHI, survival and QoL after early or delayed neurosurgery for intracranial bleeding and long-term costs of care after neurosurgery for intracranial bleeding.

Search strategy

Relevant studies will be identified through electronic searches of key databases including MEDLINE, EMBASE, Science Citation Index (SCI) and Biological Abstracts. Recent published empirical work will be used to identify optimal strategies for prognosis and diagnosis on MEDLINE and EMBASE.[25–28]

Search terms will include:

- head injur$, craniocerebral trauma (including brain injuries, coma, post-head injur, cranial nerve injuries, head injuries (closed), brain concussion, head injuries (penetrating), intracranial haemorrhage (traumatic) and skull fracture)
- clinical assessment, clinical decision rule$, guideline$, Canadian CT, CHIP, NEXUS, New Orleans, skull radiograph$, skull X-ray$, CT scanning, and hospital admission; plus such terms as
- cohort studies, longitudinal studies, follow-up studies, time factors, long term, sequela$, prognosis
- diagnostic terms such as specificity and sensitivity, false positive$, false negative$, true positive$, true negative$.

References will also be located through review of reference lists for relevant articles and through use of citation search facilities through WoK's SCI and Social Science Citation Index. Where existing systematic reviews already exist, these will be used both to identify relevant studies and to inform subsequent analysis. In addition, systematic searches of the internet the Copernic meta-search engine will be used to identify unpublished materials and work in progress. Key authors and professional and academic research groups will also be contacted and asked for unpublished material.

Review strategy

The stages of the review for diagnostic cohort studies will include:

- Accumulation of references, entry and tagging on a Reference Manager database, enabling studies to be retrieved in each of the above categories by either keyword or textword searches.
- Two reviewers will independently undertake preliminary review to identify any potentially relevant article based on titles, abstracts and subject indexing. All studies identified for inclusion, together with those for which a decision on inclusion is not possible from these brief details, will be obtained for more detailed appraisal.
- Two reviewers will make decisions on the final composition of included studies, assessed from a hard copy of the item. The decisions will be coded and recorded on the Reference Manager database by the project manager.
- Authors will be contacted, if appropriate, to clarify details and obtain missing data.
- The quality of each study will be assessed against recognised criteria.[29,30]
- Data extraction will be undertaken independently with discrepancies being discussed by the data extractors. Those that cannot be resolved at this stage will be referred to the rest of the project team.

These methods will also be used to identify studies of the management of head injuries and studies reporting data to inform the decision analysis model, but search terms, filters, selection criteria and quality assessments will be adapted to suit the purpose of each literature search.

Data extraction

The following data will be extracted from each study: population characteristics (age, gender, mechanism of injury, median GCS), setting (ED, general ward, neurosurgical centre), characteristics of the assessment or intervention (e.g. method of recording clinical features or decision score, staff training), definition of each outcome used, methods used to measure outcomes, study quality criteria (independence of the reference standard, blinding of the intervention and reference standard), prevalence of each outcome (clinically significant brain injury and need for neurosurgery), and true-positives, false-positives, false-negatives and true-positives for each outcome.

Data synthesis

Where appropriate, we will combine diagnostic data to provide pooled estimates of the diagnostic accuracy of clinical characteristics or clinical decision rules for diagnosing intracranial bleeding. For each modality, we will estimate the diagnostic performance (together with associated uncertainty) for diagnosing (1) intracranial bleeding requiring neurosurgery and (2) any clinically significant brain injury.

We will analyse data from adults and children separately wherever possible. Although we are specifically interested in diagnostic performance in patients with MHI we anticipate that most studies will report cohorts that include a range of severity. We will explore the applicability of findings to patients with MHI as part of our analysis of heterogeneity (see below).

The model used to analyse the data will depend on characteristics of the data obtained. For example, if diagnostic thresholds can be assumed constant across studies then simple methods of pooling sensitivity and specificity will be conducted.[31] If there is implicit or explicit evidence that diagnostic thresholds differ between primary studies then sensitivity and specificity cannot be considered independent and simultaneous modelling will be required.[32] A detailed assessment of heterogeneity will be conducted in all instances. If possible, meta-regression will be used to explore whether heterogeneity can be explained by study population characteristics, the method of implementation of the intervention, the definition of the outcome or the study quality, although the feasibility of this will depend on the number of individual studies identified and the quality of reporting. Where exploration of covariates is not possible or (unexplained) heterogeneity remains after the incorporation of covariates into the model(s), random effects will be incorporated to allow for such variability in results between studies.

Covariate effects, unexplainable variability and uncertainty in parameter estimates will all be reflected in the results using cutting-edge meta-analysis approaches. As the outputs from these analyses will be used in the decision modelling, all such sources of variation and uncertainty will be accurately reflected in the decision modelling.[33]

Standard meta-analysis methods will be used to combine multiple estimates, where they exist, for other parameters in the decision model.

A combination of STATA and the META-DISC statistical software[34] (version Beta 1.0.10) will be used for this analysis.

Identification of potential management strategies

We will identify potential management strategies for MHI using the following methods:

- *Literature review* As outlined above, we will identify any diagnostic management strategies evaluated in previous studies, particularly those based upon clinical decision rules.

- *Expert panel review* We will constitute an expert panel of emergency physicians, neurosurgeons and neuroradiologists, who will review emerging data from the systematic reviews and then use consensus methods to develop potential diagnostic management strategies that would be appropriate for the NHS. These may be based upon established strategies or clinical decision rules, or theoretical combinations of clinical features and diagnostic tests identified as being diagnostically useful in the systematic reviews.
- *National survey* We will undertake a national survey, as outlined below, to identify diagnostic management strategies that are currently being used in the NHS. These will then be reviewed by the expert panel and consensus methods used to select those with the potential for widespread use throughout the NHS.

National survey and routine data sources

We will undertake a national survey of EDs to identify formal guidelines used for MHI, clinical assessment strategies, policies for access to skull radiography and cranial CT, hospital admission policies (e.g. clinical decision unit, A&E observation or formal admission), bed availability, specialty responsible for inpatient care, staffing and senior supervision. This will be correlated with data from routine sources (e.g. HES).

We used a national survey in this way in our previous National Coordinating Centre for Health Technology Assessment (NCCHTA)-funded secondary research on diagnostic tests for deep vein thrombosis[35] and found it to be a valuable source of data, and well worth the relatively trivial outlay of resources required to undertake it. Data from the national survey will provide the following:

- identification of potential management strategies that are feasible in the NHS and can be evaluated by the decision-analysis model
- data to inform the structure and populate key parameters of the decision-analysis model
- context for our analysis, thus ensuring that the output of our research is relevant to the NHS.

Decision-analysis modelling

We will develop a decision-analysis model to estimate the costs and QALYs accrued by each potential management strategy for MHI, including a theoretical 'zero option' strategy of discharging all patients home without investigation. Each strategy will be applied to a theoretical cohort of patients attending the ED, with MHI allowing a direct comparison of results. For each strategy, sensitivity and specificity estimates from the literature review will determine the proportion of patients with intracranial bleeding who receive early or delayed neurosurgery and the proportion with no neurosurgical lesion who undergo diagnostic testing and/or admission to hospital.

The following costs will be estimated using data from the literature review, national survey, routine data sources and, if necessary, an expert panel: initial assessment, diagnostic tests (CT and skull radiography), hospital admission, neurosurgical intervention, long-term health and social care, and productivity losses.

Outcomes will be estimated as QALYs accrued following the decision to employ each management strategy. The expected utility associated with early or delayed neurosurgery will be taken from previous studies or, if necessary, expert panel opinion. We will search the literature to identify studies reporting survival and quality of life (QoL) after uncomplicated MHI (no bleeding), intracranial bleeding with early surgery, intracranial bleeding with delayed surgery and the disutility of the surgical procedure.

We will also use data from the Health And Long term Outcomes (HALO) study of patients with trauma. Researchers at the Medical Care Research Unit have been collecting diagnosis and baseline GCS, along with costs and QoL data up to 15 years after significant injury (including head injury). Where data from the existing literature are limited or inadequate we will ask the expert panel to review potential alternative data sources, for example extrapolating QoL data from other disabling neurological conditions. We will also use expert panel input to ensure that parameters are used in the model with appropriate estimates of uncertainty.

The time frame for the model will be the lifetime of the patient. We will assume that only patients with intracranial bleeding will incur long-term costs that are likely to be influenced by their initial diagnostic management, so long-term costs will be estimated only for patients in the model who survive intracranial bleeding. We will estimate discounted long-term costs by extrapolating follow-up costs from patients with significant head injury to the HALO study over the anticipated lifetime of the patient. Sensitivity analysis will be used to explore uncertainty in estimates of long-term costs. The baseline analysis will not include productivity losses but secondary analysis will be undertaken, including productivity losses to explore the effect of changing assumptions regarding the role of productivity losses. We will value productivity losses in the model by applying an average salary cost to estimated time off work as a result of intracranial bleeding.

We will undertake a literature review to estimate the effects of radiation exposure associated with radiological investigations (CT brain and skull radiography). We will then model these data to estimate a QALY loss and/or cost associated with each radiological investigation. This QALY loss and/or cost will then be applied to every patient in the model who receives a radiological investigation.

Analysis will be conducted in accordance with the NICE reference case.[36] Net benefit analysis will be used to identify the most cost-effective option at varying thresholds of willingness to pay.[37] The optimal strategy at the threshold currently used by NICE for decision-making will be presented as the optimal strategy for the NHS. The methodology used in the decision-analytic model will be dependent on the data that are available and the number of health states following the minor head injuries that are necessary to incorporate, with the most appropriate technique selected.

The exact modelling methodology to be used will be chosen once key data have been identified as attempting to manipulate data to fit a prespecified modelling structure will not be as accurate as choosing the method that can best represent the decision problem. The lead modeller has published papers using a wide range of decision methodologies, including discrete event simulation,[38] meta-modelling,[39] transition-state modelling,[40] decision-tree modelling,[35] and infectious disease modelling incorporating herd immunity,[41] and we are confident that whatever modelling methodology is most appropriate will be able to be constructed. If possible, we shall attempt to calibrate the mathematical model with published data during the construction phase.

Probabilistic sensitivity analyses (PSAs) will be conducted in order that any interactions and non-linearities within the modelling are properly considered. Jack-knife techniques[42] will be conducted to ensure that a sufficient number of PSA runs have been conducted to ensure that the average calculated from all runs for a management strategy is robust. Additionally the uncertainty associated in the actual mean net benefit will be provided using the percentile method in order that the full uncertainty in the results is reported. These analyses will facilitate the calculation of both full and partial expected value of perfect information, and if it is deemed appropriate an evaluation of the expected value of sample information will also be conducted.

The value of information analysis will help us to determine where funders of primary research in this important area (such as health technology assessment) should direct future studies to ensure that recommendations for policy and practice are more robust.

References

1. National Institute for Health and Clinical Excellence (NICE). *Head injury: triage, assessment, investigation and early management of head injury in infants, children and adults*. NICE clinical guideline No. 4. London: NICE; 2003.
2. National Institute for Health and Clinical Excellence (NICE). *Head injury: triage, assessment, investigation and early management of head injury in infants, children and adults*. NICE clinical guideline No. 56. London: NICE; 2007.
3. Dunning J, Stratford-Smith P, Lecky F, Batchelor J, Hogg K, Browne J, *et al.* Emergency Medicine Research Group. A meta-analysis of clinical correlates that predict significant intracranial injury in adults with minor head trauma. *J Neurotrauma* 2004;**21**:877–85.
4. Dunning J, Batchelor J, Stratford-Smith P, Teece S, Browne J, Sharpin C, *et al.* A meta-analysis of variables that predict significant intracranial injury in minor head trauma. *Arch Dis Child* 2004;**89**:653–9.
5. Stiell IG, Wells GA, Vandemheen K, Clement C, Lesiuk H, Laupacis A, *et al.* The Canadian CT Head rule for patients with minor head injury. *Lancet* 2001;**357**:1391–6.
6. Haydel MJ, Preston CA, Mills TJ, Luber S, Blaudeau E, DeBlieux PM. Indications for computed tomography in patients with minor head injury. *N Engl J Med* 2000;**343**:100–5.
7. Richless LK, English K, Heller MB, Rachlin J, McClean P, Auble TE. A prospective evaluation of radiologic criteria for head injury patients in a community emergency department. *Am J Emerg Med* 1993;**11**:327–30.
8. Miller EC, Holmes JF, Derlet RW. Utilizing clinical factors to reduce head CT scan ordering for minor head trauma patients. *J Emerg Med* 1997;**15**:453–7.
9. Stiell IG, Clement CM, Rowe BH, Schull MJ, Brison R, Cass D, *et al.* Comparison of the Canadian CT Head rule and the New Orleans criteria in patients with minor head injury. *JAMA* 2005;**294**:1511–18.
10. Smits M, Dippel DW, de Haan GG, Dekker HM, Vos PE, Kool DR, *et al.* External validation of the Canadian CT Head rule and New Orleans criteria for CT scanning in patients with minor head trauma. *JAMA* 2005;**294**:1519–25.
11. Smits M, Dippel DW, Steyerberg EW, de Haan GG, Dekker HM, Vos PE, *et al.* Predicting intracranial traumatic findings on computed tomography in patients with minor head injury: the CHIP prediction rule. *Ann Intern Med* 2007;**146**:397–405.
12. Oman JA, Cooper RJ, Holmes JF, Viccellio P, Nyce A, Ross SE, *et al.* Performance of a decision rule to predict need for CT among children with blunt head trauma. *Pediatrics* 2006;**117**:e238–46.
13. Dunning J, Daly JP, Lomas J-P, Lecky F, Batchelor K, Mackway-Jones K. Derivation of the children's head injury algorithm for the prediction of important clinical events decision rule for head injury in children. *Arch Dis Child* 2006;**91**:885–91.
14. Hofman PA, Nelemans P, Kemerink GJ, Wilmink JT. Value of radiological diagnosis of skull fracture in the management of mild head injury: meta-analysis. *J Neurol Neurosurg Psychiatry* 2000;**68**:416–22.

15. Kelly AB, Zimmerman RD, Snow RB, Gandy SE, Heier LBA, Deck MDF. Head trauma – comparison of MR and CT – experience of 100 patients. *Am J Neuroradiol* 1988;**9**:699–708.

16. Ingebrigtsen T. Routine early CT-scan is cost saving after minor head injury. *Acta Neurol Scand* 1996;**93**:207–10.

17. Af Geijerstam J-L, Britton M, Marke LA. Minor head injury: observation or computer tomography? Economic aspects by literature review and economic analysis. *Emerg Med J* 2004;**21**:54–8.

18. Norlund A, Marke LA, af Geijerstam J-L Oredsson S, Britton M and the OCTOPUS study investigators. Immediate computed tomography or admission for observation after mild head injury: cost comparison in randomised controlled trial. *BMJ* 2006;**333**:469.

19. Af Geijerstam J-L, Oredsson S, Britton M and the OCTOPUS study investigators. Medical outcome after immediate computed tomography or admission for observation in patients with mild head injury: randomised controlled trial. *BMJ* 2006;**333**:465–8.

20. Stein SC. Indications for CT scanning in mild traumatic brain injury: a cost-effectiveness study. *J Trauma* 2006;**61**:558–66.

21. Sultan HY, Boyle A, Pereira M, *et al.* Application of the Canadian CT head rules in managing minor head injuries in a UK emergency department: implications for the implementation of the NICE guidelines. *Emerg Med J* 2004;**21**:420–5.

22. Hassan Z, Smith M, Littlewood S, Bouamra O, Hughes D, Biggin C, *et al.* Head injuries: a study evaluating the impact of the NICE head injury guidelines. *Emerg Med J* 2005;**22**:845–9.

23. Shravat BP, Hynes KA. The impact of NICE guidelines for the management of head injury on the workload of the radiology department. *Emerg Med J* 2004;**21**:521–2.

24. Goodacre S. Hospital admissions with head injury following publication of NICE guidance. *Emerg Med J* 2008;**25**:556–7.

25. Westwood ME, Whiting PF, Kleijen J. How does study quality affect the results of a diagnostic meta-analysis? *BMC Med Res Methodol* 2005;**5**:20.

26. Whiting P, Harbord R, Kleijnen J. No role for quality scores in systematic reviews of diagnostic accuracy studies. *BMC Med Res Methodol* 2005;**5**:19.

27. Whiting P, Rutjes AW, Dinnes J, Reitsma JB, Bossuyt PM, Kleijnen J. A systematic review finds that diagnostic reviews fail to incorporate quality despite available tools. *J Clin Epidemiol* 2005;**58**:1–12.

28. Whiting P, Rutjes AW, Dinnes J, Reitsma J, Bossuyt PM, Kleijnen J. Development and validation of methods for assessing the quality of diagnostic accuracy studies. *Health Technol Assess* 2004;**8**(25).

29. Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, *et al. Towards complete and accurate reporting of studies of diagnostic accuracy: The STARD initiative*. Department of Clinical Epidemiology and Biostatistics Academic Medical Centre, University of Amsterdam, the Netherlands; 2003.

30. Lijmer JG, Mol JJ, Heisterkamp S, Bonsel GJ, van der Meulen JHP, Bossuyt PMM. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999;**282**:1061–6.

31. Deeks JJ. Systematic reviews of evaluations of diagnostic and screening tests. In Egger M, Davey Smith G, Altman DG (editors). *Systematic reviews in health care: meta-analysis in context*. 2nd edn. London: BMJ Publishing Group; 2001.

32. Harbord RM, Deeks JJ, Egger M, Whiting P, Sterne JA. A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics* 2007;**8**:239–51.

33. Sutton AJ, Cooper NJ, Goodacre S, Stevenson M. Integration of meta-analysis and economic decision modelling for evaluating diagnostic tests. *Med Decis Making* 2008;**28**:650–67.

34. Zamora J, Abraira V, Muriel A, Khan KS, Coomavasamy A. Meta-DiSc: a software for meta-analysis of test accuracy data. *BMC Med Res Methodol* 2006;**6**:31.

35. Goodacre S, Sampson F, Stevenson M, Wailoo A, Sutton AJ, Thomas S, *et al.* Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis. *Health Technol Assess* 2006;**10**(15).

36. National Institute of Clinical Excellence (NICE). *Guide to the methods of technology appraisal*. London: NICE; 2004.

37. Fenwick E, Claxton K, Sculpher M (2001). Representing uncertainty: the role of cost-effectiveness acceptability curves. *Health Econ* 10:779–87.

38. Stevenson MD, Oakley JE, Chick SE, Chalkidou K. The cost-effectiveness of surgical instrument management policies to reduce the risk of vCJD transmission to humans. *JORS* 2009;**60**:506–18.

39. Stevenson MD, Brazier JE, Calvert NW, Lloyd-Jones M, Oakley J, Kanis JA. Description of an individual patient methodology for calculating the cost-effectiveness of treatments for osteoporosis in women. *JORS* 2005;**56**:214–21.

40. Wardlaw JM, Chappell FM, Stevenson M, De Nigris E, Thomas S, Gillard J, *et al.* Accurate, practical and cost-effective assessment of carotid stenosis in the UK. *Health Technol Assess* 2006;**10**(30).

41. Stevenson MD, Beard SM, Finn A, Brennan A. Estimating the potential health gain and cost consequences of introducing a pre-school pertussis booster into the UK child vaccination schedule. *Vaccine* 2002;**20**:1778–86.

42. Inglehart DL. Simulating stable stochastic systems, V: comparison of ratio estimators. *Naval Res Logist Quart* 1975;**22**:553–65.

Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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