

Research

Accuracy of the Canadian C-spine rule and NEXUS to screen for clinically important cervical spine injury in patients following blunt trauma: a systematic review

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Abstract

Background: There is uncertainty about the optimal approach to screen for clinically important cervical spine (C-spine) injury following blunt trauma. We conducted a systematic review to investigate the diagnostic accuracy of the Canadian C-spine rule and the National Emergency X-Radiography Utilization Study (NEXUS) criteria, 2 rules that are available to assist emergency physicians to assess the need for cervical spine imaging.

Methods: We identified studies by an electronic search of CINAHL, Embase and MED-LINE. We included articles that reported on a cohort of patients who experienced blunt trauma and for whom clinically important cervical spine injury detectable by diagnostic imaging was the differential diagnosis; evaluated the diagnostic accuracy of the Canadian C-spine rule or NEXUS or both; and used an adequate reference standard. We assessed the methodologic quality using the Quality Assessment of Diagnostic Accuracy Studies criteria. We used the extracted data to calculate sensitivity, specificity, likelihood ratios and post-test probabilities.

Results: We included 15 studies of modest methodologic quality. For the Canadian C-spine rule, sensitivity ranged from 0.90 to 1.00 and specificity ranged from 0.01 to 0.77. For NEXUS, sensitivity ranged from 0.02 to 0.46. One study directly compared the accuracy of these 2 rules using the same cohort and found that the Canadian C-spine rule had better accuracy. For both rules, a negative test was more informative for reducing the probability of a clinically important cervical spine injury.

Interpretation: Based on studies with modest methodologic quality and only one direct comparison, we found that the Canadian Cspine rule appears to have better diagnostic accuracy than the NEXUS criteria. Future studies need to follow rigorous methodologic procedures to ensure that the findings are as free of bias as possible. **Competing interests:** None declared.

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clinically important cervical spine injury is defined as any fracture, dislocation or ligamentous instability detectable by diagnostic imaging and requiring surgical or specialist follow-up.^{1,2} These injuries can have disastrous consequences including spinal cord injury and death if the diagnosis is delayed or missed.³ Despite the low prevalence (< 3%) of clinically important cervical spinal injury following blunt trauma (e.g., motor vehicle collision), accurate diagnosis is imperative for safe, effective management.⁴ Currently, uncertainty exists about the optimal diagnostic approach. Some guidelines^{5,6} advocate using screening tools to identify patients with a higher likelihood of clinically important cervical spinal injury; these patients are then sent for imaging to establish the diagnosis. In other more conservative settings, all patients with blunt trauma are sent for imaging. The first approach, involving screening, is arguably preferable because it optimizes resources and time, while reducing unnecessary costs, radiation exposure and psychological stress for the patient.⁷ For screening to be safe and effective, the screening tools must have high sensitivity, a low negative likelihood ratio and a low rate of false positives. This assures clinicians that a clinically important cervical spine injury is unlikely and reduces the number of referrals for imaging.

Clinical decision rules synthesize 3 or more findings from the patient's history, physical examination or simple diagnostic tests to guide diagnostic and treatment decisions.89 Two clinical decision rules, the Canadian C-spine rule² and the National Emergency X-Radiography Utilization Study (NEXUS; Box 1),10 are available to assess the need for imaging in patients with cervical spine injury following blunt trauma. These rules aim to reduce unnecessary imaging by reserving these investigations for patients with a higher likelihood of clinically important cervical spinal injury. Developed independently and validated using large cohorts of patients, these 2 decision rules are recommended in many international guidelines.^{5,11,12} However, no consensus exists as to which rule should be endorsed.¹²⁻¹⁴ Therefore, the purpose of our systematic review was to describe the quality of research evaluating the Canadian C-spine rule and NEXUS; describe the diagnostic accuracy of the Canadian C-spine rule and NEXUS; and compare the diagnostic accuracy of the Canadian C-spine rule to that of NEXUS.

Methods

Data sources

Three electronic databases (CINAHL, Embase, MEDLINE) were searched from inception until Sept. 12, 2011. The search strategy consisted of terms describing the Canadian C-spine rule and NEXUS (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.120675/-/DC1). We did not use a diagnostic search filter because even sensitive filters can miss relevant studies and perform inconsistently.¹⁵ We screened the reference lists of included studies and related systematic reviews to identify diagnostic studies missed by the database search.

Study selection

Two reviewers (Z.M and C.M., A.V., T.R. or C.-W.L.) independently applied selection criteria to titles and abstracts and then full papers. We included articles that met the following criteria: reported on a cohort of patients presenting with

Box 1: National Emergency X-Radiography Utilization Study (NEXUS) low-risk criteria¹⁰

Cervical spine radiography is indicated for patients with neck trauma unless they meet ALL of the following criteria:

- No posterior midline cervical-spine tenderness
- No evidence of intoxication
- A normal level of alertness (score of 15 on the Glasgow Coma Scale)
- No focal neurologic deficit
- No painful distracting injuries

symptoms of cervical spine injury following blunt trauma and clinically important cervical spine injury was a differential diagnosis; evaluated the diagnostic performance of the Canadian C-spine rule or NEXUS criteria; confirmed the diagnosis of clinically important spinal injury with an adequate reference standard (e.g., plain radiographs, computed tomography, magnetic resonance imaging); and reported results in sufficient detail to allow reconstruction of contingency tables. No language restriction was applied.

Quality assessment

Two reviewers (Z.M. and A.V., T.R. or C.-W.L.) assessed the methodologic quality of studies using the 11-item Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria.¹⁶ Studies were included regardless of their risk of bias.¹⁶ Disagreements were resolved first in discussion (Z.M. and A.V., T.R. or C.-W.L.), and then by an independent third reviewer if necessary (C.M.). The inter-rater reliability of the quality assessment was evaluated using percentage agreement and Kappa (K) statistics.

Data extraction and analysis

Two authors (Z.M. and C.M., A.V., T.R. or C.-W.L) independently extracted data, including the number of participants, setting, characteristics of the index test and reference standard, prevalence of clinically important cervical spinal injury, and raw data to enable reconstruction of contingency tables. We added 0.5 to the empty cells in the contingency table when a computational problem existed and calculated sensitivity, specificity, likelihood ratios, post-test probabilities and percentage of true negative test results. We planned to pool sensitivity and specificity using a bivariate model if included studies showed sufficient clinical and statistical homogeneity.^{17,18} We conducted a sensitivity analysis to evaluate the diagnostic performance of the Canadian C-spine rule and NEXUS using studies that assessed the rule prospectively and in their entirety.

Results

Our search retrieved 578 articles. Fifteen studies were included after screening (Figure 1) and all were published in English. Eight studies evaluated the Canadian C-spine rule alone^{2,19-25} and 6 studies evaluated NEXUS alone.^{7,10,26-29} We considered only one of the studies to be a direct comparison, because the diagnostic accuracy of both rules were evaluated prospectively in the same patients and by the same physicians.¹³ The other comparison was reported in 2 separate

studies and evaluated the rules using different study designs and assessors.^{2,26} We did not consider this to be an accurate direct comparison of the 2 rules, hence we presented these studies individually.^{2,26} The prevalence of clinically important spinal injury ranged from 0.4%¹⁹ to 6%^{25,28} (median 1.95%, interquartile range [IQR] 1.13-2.74) and included injuries such as C1 arch fracture, C2 hangman's fracture and C6/7 fracture/subluxation, all of which required surgical intervention, specialist follow-up, or both. Table 1 outlines the characteristics of the included studies. Based on visual inspection of forest plots and statistical testing (a statistically significant χ^2 and moderate-to-high I^2 value), we determined that the included studies were too heterogeneous to pool.

The quality, percentage agreement and κ statistic for the QUADAS items are shown in Table 2. Inter-rater reliability was slight to poor for most items, with one item having moderate reliability. No disagreement persisted between reviewers after the consensus meeting. The included studies were of modest quality. Only 6 studies reported enrolment of consecutive patients, highlighting potential selection bias in the remaining 9 studies.

Six studies used a "gold standard" reference test for all patients;^{7,10,25,27,28} the remaining 9 studies were influenced by differential verification bias because not all patients underwent imaging or patients underwent different reference tests at the discretion of the treating physician. In the 8 studies that used different reference tests, patients who did not undergo imaging were followed up with either the 14-day proxy2,13,19,22,23,26 or the 21-day surveillance strategy.^{19,21,24} With the 14-day proxy method, patients are contacted by a registered nurse 14 days after discharge and asked 8 questions about pain and return to function. A positive response to these questions resulted in patients being asked to return to hospital for imaging investigations. With the 21-day surveillance strategy, patient logs at major hospitals and neurosurgical centres were monitored for readmission.

Canadian C-spine rule

Of the 9 studies that assessed the Canadian Cspine rule, 4 were prospective studies^{2,13,21,23} that aimed to assess the rule in its entirety; 4 prospectively applied a modified version of the rule;^{19,22,24,25} and 1 was a retrospective study.²⁰ The sensitivity of the Canadian C-spine rule ranged from 0.90 to 1.0, while the specificity ranged from 0.01 to 0.77 (Figure 2). The Canadian C-spine rule had a low rate of false negative results (0%–0.11%),²⁴ and imaging rates would have been reduced by an average of 42.0% (0.6%-75.4%) without missing a clinically important cervical spine injury. Figure 3 shows the prevalence of clinically important injury reported in each study, positive and negative likelihood ratios and the post-test probability given a positive and negative test result. The median negative likelihood ratios of 0.18 (IQR 0.03-0.24) were more informative than the median positive likelihood ratios of 1.69 (IQR 1.57-1.81). Given the low prevalence of clinically important spinal injury (median 1.95%), a positive response to the Canadian C-spine rule only increased the post-probability to 2.4% (IQR 1.30%–5.85%), while a negative test result was more informative because it reduced the postprobability to 0.16% (IQR 0.38%-3.08%).

Four studies^{2,13,21,23} were included in the sensitivity analysis. This analysis reaffirmed that the Canadian C-spine rule is highly sensitive (range 0.99–1.00) and significantly reduced the range over which specificity spanned (range 0.42–0.45).

NEXUS

Seven studies assessed the NEXUS rule. Of the 5 prospective studies, 4 assessed the rule in its entirety^{10,13,28,29} and 1 assessed a modified version (adding 7 questions from the Clinical sobriety

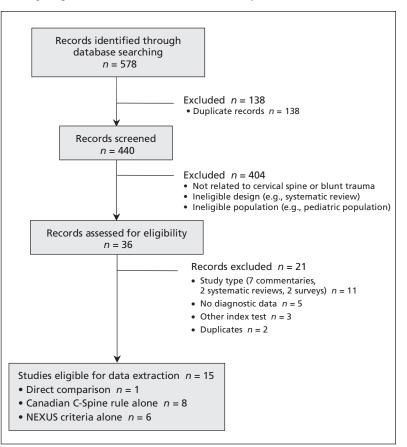


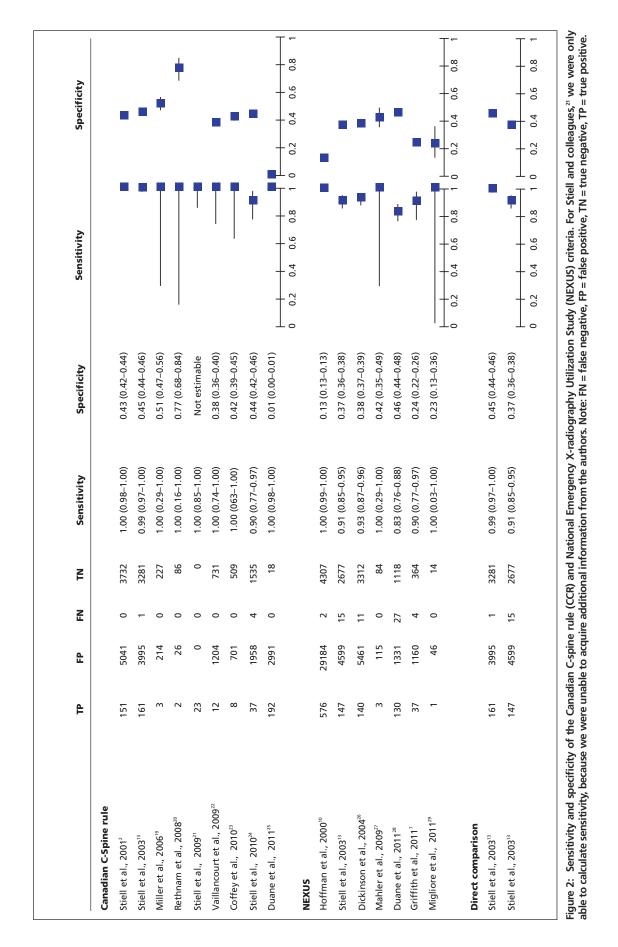
Figure 1: Flow diagram of studies selected for inclusion.

Design Country N Male Male Male MOI Index text Reference standard (% of patients who received it) Prospective US 34.069 64.8 NR • Index: NEXUS • Radiography: minimum 3 views; additional views/inwestigations ordered at the discretion of treating physician Prospective Canada 8.24 51.5 M/C • Index: Canadian C-spine rule additional views/inwestigations ordered at the discretion of treating physician • Radiography ordered at the discretion of the treating physician (83.9) Prospective Canada 8.24 51.5 M/C • Index: Canadian C-spine rule additional views/inwestigations ordered at the discretion of the treating physician (83.9) • Index: additional views/inwestigations ordered at the discretion of the treating physician (83.9) Prospective Canada 8.24 51.5 M/C • Index: Canadian C-spine rule of the treating physician (71.7) • Index additional views/inwestigations ordered at the discretion of the treating physician (83.9) Prospective Canada 8.24 51.5 M/C • Index: Canadian C-spine rule of the treating physician (83.9) • Index additional views/inwestigations ordered of the treating physician (83.9) Prospective UK Alobe Fraining: ves						2			
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Prospective cross-sectional Ganda 8/24 5/15 MVC Index: Canadian C-spine rule cross-sectional Realiography ordered at the discretion resident emergency physician, supervised (if the treating physician (68.9)) Prospective cross-sectional Ganda 8/23 Garda - Assessors: emergency physician, supervised resident emergency medicine physician (71.7) - Adda proxy (31.1) Prospective cross-sectional Ganda 8/24 5/15 MVC - Adda proxy medicine physician (71.7) Prospective cross-sectional Ganda 8/24 5/15 MVC - Adda proxy (31.1) Retrospective cross-sectional Ganda 8/24 5/15 MVC - Index: S NEXUS items approximated from physician, supervised - Addiography and computed or othered at the discretion Retrospective data from stiell 2001 ⁴ B/24 5/15 MVC - Index: S NEXUS items approximated from physician (51.2) - Addiography and computed or othered at the discretion Prospective data from stiell 2001 ⁴ Hodo NR - Index: S NEXUS items approximated from cross-sectional - Addiography and computed or othered at the discretion Prospective erview UK 4/60 NR - Index: Canadian C-spine rule for treadion C-spi	Hoffman et al., 2000 ¹⁰		US	34 069	64.8	NR	 Index: NEXUS Assessors: emergency physician Training: yes 	 Radiography: minimum 3 views; additional views/investigations ordered at the discretion of treating physician (100) 	0
Prospective Prospective Conssectional Conssectional Conssectional ConssectionalReadiography ordered at the discretion of the treating physicians of the treating physician (71.7)Cross-sectional Conssectional8.2451.5MVCendexes consident emergency medicine of the treating physician (63.9)Retrospective Canada8.2451.5MVCendexes conserting physicians, supervised of the treating physician (63.9)Retrospective CanadaUK460NRNRendered at the discretion of the treating physician (63.9)Prospective ConssectionalUK460NRNRendered at the discretion of the treating physician (63.9)Prospective ConssectionalUK460NRNRendered at the discretion of the treating physician (63.9)Prospective ConssectionalUK10NRNRendered at the discretion of the treating physician (63.9)Prospective ConssectionalUK10NRNRendered at the discretion of the treating physician (63.9)Prospective ConssectionalUK114NRNRendered at the discretion of the treating physician (63.9)Retrospective ConssectionalUK114NRNRendered at the discretion of the treating physician (63.9)Prospective ConssectionalUKNRNRIndex: Canadian C-spine rule of the treating physician (43)Prospective ConssectionalUKNRNRIndex: Anostrospication of canadian C-spine ruleProspective Conssectional </td <td>Stiell et al., 2001²</td> <td></td> <td>Canada</td> <td>8 924</td> <td>51.5</td> <td>MVC 67%</td> <td> Index: Canadian C-spine rule Assessors: emergency physicians, supervised residents Training: yes </td> <td> Radiography ordered at the discretion of the treating physician (68.9) 14-day proxy (31.1) </td> <td>577 (6.5)</td>	Stiell et al., 2001²		Canada	8 924	51.5	MVC 67%	 Index: Canadian C-spine rule Assessors: emergency physicians, supervised residents Training: yes 	 Radiography ordered at the discretion of the treating physician (68.9) 14-day proxy (31.1) 	577 (6.5)
Retrospective analysis of data from Stell 20011 ¹² 8 92451.5MVCIndex: 5 NEXUS items approximated from to findex: 5 NEXUS items collected prospectively of the treating physician (68.9) 1-4.day proxy (31.1)Atta from tata from stell 2001 ¹² UK460NRIndex: 5 NEXUS items collected prospectively of the treating physician (68.9)Prospective prospective by to sossectionalUK460NRIndex: 5 NEXUS items collected prospective discretion of the treating physician (45)Prospective to sossectionalUK114NRNRIndex: 5 NEXUS items approximated from of the treating physician (45)Retrospective to sossectionalUK114NRNRIndex: 5 NEXUS items and items of the treating physician (45)Retrospective to sossectionalUK114NRNRIndex: 5 NEXUS items and items of the treating physician (45)Retrospective to sossectionalUK114NRNRIndex: 5 NEXUS items and items of the treating physician (45)Retrospective to sossectionalUK114NRNRIndex: 5 NEXUS items and items of the treating physician (45)Retrospective to sossectiveUKNRNRIndex: 5 NEXUS items and clinical sobriety of the treating physician (45)Retrospective to sossectionalUKNRNRIndex: 5 NEXUS items and cl	Stiell et al., 2003 ¹³		Canada	8 283	52.3	MVC 67.2%	 Index: Canadian C-spine rule and NEXUS Assessors: resident emergency medicine physicians Training: yes 	 Radiography ordered at the discretion of the treating physician (71.7) 14-day proxy (28.2) 	854 (10.3) indeterminate cases not included in the analysis
Prospective cross-sectionalUK460NRIndex: Canadian C-spine rule for immobilization• Radiography ordered at the discretion of the treating physician (45)cross-sectional cross-sectionalUK114NR• Assessors: nursing staff all grades • Training: yes• 14-day proxy, no. not reported • 21-day surveillance, no. not reported 	Dickinson et al., 2004 ²⁶	Retrospective analysis of data from Stiell 2001 ¹²	Canada	8 924	51.5	MVC 67%	 Index: 5 NEXUS items approximated from 20-items collected prospectively Assessors: emergency physicians, supervised residents Training: yes 	 Radiography and computed tomography ordered at the discretion of the treating physician (68.9) 14-day proxy (31.1) 	577 (6.5)
Retrospective UK 114 NR Index: Canadian C-spine rule • Only patients who had cervical spine review • Assessors: retrospective application of • Only patients who had cervical spine review • Assessors: retrospective application of • Only patients who had cervical spine review • Assessors: retrospective application of • Only patients who had cervical spine review • Assessors: retrospective application of • Assessors: retrospective D • N • Training: NR • All patients underwent computed cross-sectional • Assessors: emergency physicians • All patients underwent computed • Assessors: emergency physicians • Training: NR • Training: NR	Miller et al. 2006 ¹⁹	, Prospective cross-sectional	UK	460	R	NR	 Index: Canadian C-spine rule for immobilization Assessors: nursing staff all grades Training: yes 	 Radiography ordered at the discretion of the treating physician (45) 14-day proxy, no. not reported 21-day surveillance, no. not reported 	N
Prospective US 202 NR Index: 4 NEXUS items and clinical sobriety • All patients underwent computed assessment tool (7 questions) cross-sectional assessment tool (7 questions) tomography (100) • Assessors: emergency physicians • Training: NR	Rethnam ei al., 2008² [°]		ЧK	114	R	R	 Index: Canadian C-spine rule Assessors: retrospective application of Canadian C-spine rule Training: NR 	 Only patients who had cervical spine radiographs were included. 	N/A, patients were included if radiography was conducted
	Mahler et al., 2009² ⁷	Prospective cross-sectional	US	202	R	NR	 Index: 4 NEXUS items and clinical sobriety assessment tool (7 questions) Assessors: emergency physicians Training: NR 	 All patients underwent computed tomography (100) 	0

Table 1 (pa	Table 1 (part 2 of 2): Characteristics of the included studies	acteristics o	f the inclu	uded stu	dies			
Study	Design	Country	N	% Male	IOM	Index test	Reference standard (% of patients who received it)	No. of patients lost to follow- up (%)
Stiell et al, 2009²¹	Prospective cross-sectional	Canada	3 628	51.0	MVC 70.1%	 Index: Canadian C-spine rule Assessors: emergency physicians. Training: yes 	 Radiography ordered at the discretion of the treating physician (53.3) 30 day surveillance of ED and neurosurgical centres 	Radiography conducted in 47.2% of patients
Vaillancour et al., 2009²	Vaillancourt Prospective et al., 2009 ²² cross-sectional	Canada	2 393	50.2	MVC 62.5%	 Index: Canadian C-spine rule revised for paramedics[†] Assessors: paramedics Training: yes 	 Radiography ordered at the discretion of the treating physician (52.9) 14-day proxy (28.5) 	444 (18.6)
Coffey et al., 2010 ²³	Prospective cross-sectional	NK	1 420	50.4	MVC 75.8%	 Index: Canadian C-spine rule Assessor: emergency physicians of all grades Training: yes 	 Radiography ordered at the discretion of the treating physician (69.5) 14-day proxy (18) 	178 (12.5)
Stiell et al., 2010 ²⁴	Prospective cross-sectional	Canada	3 633	46.4	MVC 63%	 Index: Canadian C-spine rule for immobilization Assessors: experienced nurses in emergency department Training: yes 	 Radiography ordered at the discretion of the treating physician (47.2) 30-day surveillance of ED and neurosurgical centres 	Radiography conducted in 47.2% of patients
Duane et al., 2011 ²⁵	Prospective cross-sectional	N	3 201	64	NR	 Index: approximation of Canadian C-spine rule (minus rotation) Assessors: residents Training: yes‡ 	 All patients underwent computed tomography (100) 	0
Duane et al., 2011² ^s	Prospective cross-sectional	US	2 606	65	MVC, % NR	 Index: NEXUS Assessors: residents Training: yes‡ 	 All patients underwent computed tomography (100) 	0
Griffith et al., 2011 ⁷	Retrospective analysis from radiology information record system	US	1 589	59.3	MVC 37.7%	 Index: NEXUS Assessors: 2nd and 3rd year radiology students Training: evaluation of clinical records 	 Only patients who underwent cervical spine computed tomography were included. 	NA, patients were included if computed tomography was conducted
Migliore et al., 2011 ²⁹	Prospective cross-sectional	N	80	NR	NR	 Index: NEXUS Assessors: physicians, residents Training: NR 	 Radiography or computed tomography (75) 	10 (15)
Note: CT = comput NR = not reported. †The item "delayee ‡Residents received	Note: CT = computed tomography, ED = Emergency department, MOI = Mechanism of in NR = not reported. #The item "delayed onset of neck pain" was excluded because paramedics would assess #Residents received a 5-min explanation as to using a standardized data collection form.	, ED = Emerger oain" was excl ation as to usi	ncy departn luded becau ing a standa	nent, MOI ise parame ardized dat	= Mechanis dics would ta collectior	Note: CT = computed tomography, ED = Emergency department, MOI = Mechanism of injury, MVC = motor vehicle collision, NA = not applicable; NEXUS = National X-radiography Utilization Study low risk criteria. NR = not reported. The item "delayed onset of neck pain" was excluded because paramedics would assess patients before such delay. #Residents received a 5-min explanation as to using a standarclized data collection form.	ole; NEXUS = National X-radiography Utilization Study k	ow risk criteria,

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Study	Selection bias*	Reference test†‡	Disease progression§	Partial verification bias¶	Differential verification bias**	Incorporation biast†	Reference reviewer bias‡‡	Index reviewer bias§§	Clinical review bias¶¶	Uninterpretable results***	Withdrawals†††
Hoffman et al., 2000 ¹⁰	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Stiell et al., 2001 ²	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes
Stiell et al., 2003 ¹³	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear
Dickinson et al., 2004 ²⁶	Yes	Yes	Unclear	Yes	No	Yes	Yes	Unclear	Yes	Yes	NA
Miller et al., 2006 ¹⁹	Yes	Yes	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Yes
Rethnam et al., 2008 ²⁰	No	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	No	NA
Mahler et al., 2009 ²⁷	No	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes
Stiell et al., 2009 ²¹	Yes	No	No	No	No	Yes	Unclear	Yes	Yes	No	No
Vaillancourt et al., 2009 ²	No	Yes	Yes	No	No	Unclear	Unclear	Unclear	Yes	Yes	Yes
Coffey et al., 2010 ²³	Yes	Yes	Yes	No	No	Unclear	Unclear	Unclear	Yes	Yes	Yes
Stiell et al., 2010 ²⁴	Yes	No	No*	No	No	Yes	Unclear	Unclear	Yes	Yes	Yes
Duane et al., 2011 ²⁵	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Duane et al., 2011 ²⁸	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Griffith et al., 2011^7	No	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	NA
Migliore et al., 2011 ²⁹	No	Yes	Unclear	No	No	Unclear	Unclear	Yes	Yes	No	No
Inter-rater reliability, K	0.54	0.00	0.15	-0.13	0.21	0.47	0.39	0.17	-0.03	-0.02	0.00
Percentage agreement, %	73	87	53	47	53	80	67	53	87	53	33
Note: NA = not applicable. *Was the spectrum of patients representative of the patients who will receive the test in practice? Is it a selective sample of patients? *Was the spectrum of patients representative of the patients who will receive the test in practice? Is it a selective sample of patients? The 14-day proxy method was deemed to be an adequate reference standard because the outcome for all patients could be accounted for by either by the 14-day proxy method or radiography. This mirrors clinical practice. ³⁴ However, the 21-day surveillance strategy to support its use as a reference standard. Sis the time between the reference standard because the outcome for all patients with fractures missed at the initial presentation would be subsequently aptured in patient logs. We found no data about the accuracy of the 21-day surveillance strategy to support its use as a reference standard. Sis the time between the reference standard regardless of the 21-day surveillance strategy to support its use as a reference standard. The woole sample, or a random selection of the azumele, receive verification using a reference standard of diagnosis? The woole sample or a redom selection of the angle, receive verification using a reference standard)? The same reference standard regardless of the index test result? This the reference standard regults of the index test results of the index test results interpreted without knowledge of the results of the index test results of the results of the reference standard? These the reference standard regret when the next results of the reference standard? The standard data available when the index test results of the reference standard? The standard results interpreted without knowledge of	representati representati y to classify t s deemed to l s urveillance und no data nund nund represed un s vailable whe	ve of the patie the target cond be an adequati strategy was d about the acci d and the index tandard regarc of the index te preted withour thout knowled en the index te tet test results i	nts who will receiv lition correctly? = reference standa leemed to be an in leracy of the 21-day w test short enough lie, receive verifica lies of the index t t knowledge of the results were inte eported?	ceive the test in practice? Is it and the test in practice? Is it inder because the outcome for inadequate reference stand day surveillance strategy to si uigh to be reasonably sure tha firstion using a reference star stest result? Lex test did not form part of th f the results of the index test? It of the reference standard? interpreted as would be avail	ceive the test in practice? Is it a selective sample of pa dard because the outcome for all patients could be a indard because the outcome for all patients could be a day survellance strategy to support its use as a refer- ough to be reasonably sure that the target condition fication using a reference standard of diagnosis? fication using a reference standard of fication using a reference standard of fication using a reference standard of fice tresult? Its of the reference standard? Its of the reference standard? Its of the reference standard? Its of the reference standard?	ceive the test in practice? Is it a selective sample of patients? A dard because the outcome for all patients could be accounted for t indequate reference standard because it assumes that patients we day surveillance strategy to support its use as a reference standard. Unply to be reasonably sure that the target condition did not change fication using a reference standard of diagnosis? Ex test result? Its vest did not form part of the reference standard)? Its of the reference standard? Its of the reference standard? Its of the reference standard? Its of the reference standard? Its of the reference standard?	ents? ents? counted for by ei at patients with f ce standard. J not change beth 1 in practice?	ther by the 14-da ractures missed a ween the 2 tests?	y proxy method t the initial pres	or radiography. This r entation would be sul	nirrors clinical ssequently



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assessment tool).27 Two were retrospective studies.7,26 The sensitivity of NEXUS ranged from 0.83 to 1.0, while the specificity ranged from 0.13 to 0.46 (Figure 2). Similar to the Canadian C-spine rule, the negative likelihood ratio (median 0.30, IQR 0.19-0.41) was more informative than the positive likelihood ratio (median 1.44, IQR 1.14-1.52) (Figure 3). In contrast, most of the NEXUS studies did not report large shifts in the post-test probability of clinically important injury from the prevalence (median 1.95%) with a positive test result (median posttest probability 3.10%, IQR 2.50%-3.10%) or negative test result (median post-test probability 0.60%, IQR 0.30%-2.40%). False negatives for NEXUS ranged from 0% to 1.0%,⁷ and imaging rates would have been reduced by an average of 30.9% (range 12.6%¹⁰ to 42.9%²⁸) without missing a clinically important cervical spine injury. The findings by Migliore and colleagues²⁹ should be interpreted with caution because this small study was of low methodologic quality

and the data yield counterintuitive likelihood ratios (positive liklihood ratio < 1.0, negative liklihood ratio > 1.0). Only data for the residents, and not emergency physicians, were reported because these 2 groups are not statistically independent and the results for the emergency physicians appeared unreliable because all study participants were sent for imaging. Four studies^{10,13,28,29} were included in the sensitivity analysis, and these results were consistent with the primary analysis.

Direct comparison of the Canadian C-spine rule and NEXUS

The only direct comparison of the 2 rules indicates that the Canadian C-spine rule has better diagnostic accuracy, as shown by nonoverlapping 95% confidence intervals for sensitivity, specificity and the likelihood ratios (Figures 2 and 3).¹³ The Canadian C-Spine rule would have reduced imaging rates by 44%, while NEXUS would have reduced the rates by 36%.

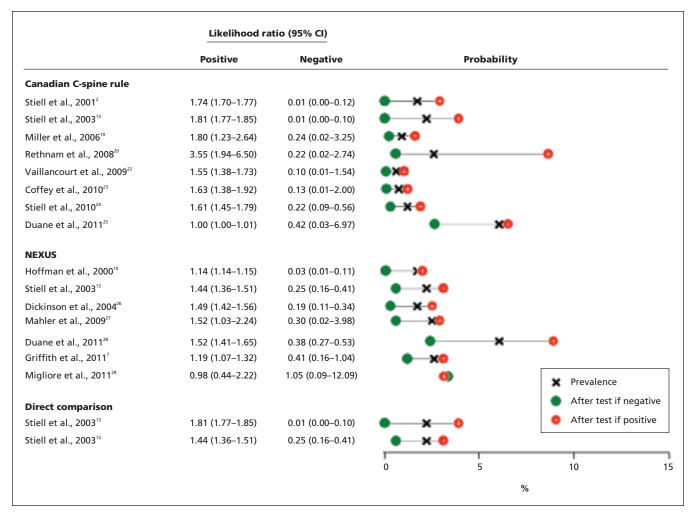


Figure 3: Probability of clinically important cervical spinal injury and likelihood ratios for the Canadian C-spine rule and National Emergency X-Radiography Utilization Study (NEXUS) criteria. For Stiell and colleagues,²¹ we were only able to calculate sensitivity, because we were unable to acquire additional information from the authors.

Interpretation

We found 15 studies of modest methodologic quality that evaluated the diagnostic accuracy of the Canadian C-spine rule and NEXUS. We found that both rules had consistently high sensitivity, indicating that a negative test result is highly informative in excluding a clinically important cervical spine injury and, therefore, the need for radiographic examination. The value of a negative test result is further shown by the low negative likelihood ratio and post-test probability. In the only direct comparison, the Canadian Cspine rule had higher sensitivity, and thus gives fewer false negative results. Because both rules are based on imaging all patients with positive results, the low specificity and high false positive rate means that many people without injury will undergo unnecessary imaging. The results of the sensitivity analysis reinforced the primary findings. However, for the Canadian C-spine rule, the range over which specificity spanned was significantly reduced. This suggests that the diagnostic accuracy of the Canadian C-spine rule is superior when the rule is used in its entirety.

The findings of this review are consistent with a previous meta-analysis¹⁴ and 2 literature reviews.^{30,31} However, our review used a larger and more sensitive search strategy, which resulted in a larger number of primary studies identified for inclusion. In addition, we considered the methodologic quality of the included studies when interpreting the diagnostic accuracy. As a result, we have outlined an optimal diagnostic study design for future studies in this area (Appendix 2, available at www.cmaj.ca /lookup/suppl/doi:10.1503/cmaj.120675/-/DC1) in order to reduce potential biases.

Clinically, our review highlights the effectiveness of the Canadian C-spine rule and NEXUS in clearing the cervical spine without the need for imaging, while maintaining patient safety. Although most of the studies included in this review are validation studies, only the Canadian C-Spine rule has been evaluated in an impact analysis study, which further supports its use in practice.²¹ Despite these findings, there is a more liberal use of imaging in current clinical practice, which may reflect patient preference, physicians' fear of litigation or missing a fracture, or uncertainty of the application or accuracy of the screening tools. Improved education of physicians may facilitate greater use of these rules. In particular, educational content should focus on the subjective components of the Canadian Cspine rule (e.g., dangerous mechanism of injury,²¹ range of motion assessment) and NEXUS (e.g., distracting injuries, intoxication)32 because these components were most frequently misinterpreted.

Educating patients may also improve the utilization of these screening tools. In the absence of any clinical indication of a clinically important cervical spinal injury, routine imaging is not associated with psychological benefits or improved outcomes.33 Patients knowledge of this, together with knowledge about the accuracy of these screening tools weighed against the potential harms of unnecessary radiation exposure, would allow for more informed decisions to be made. To ease the concerns of patients discharged without imaging, further evaluation of alternate follow-up strategies, such as the 14-day proxy, would be beneficial for both clinical practice and research. Currently there is only limited data to support the use of the 14-day proxy as a reference standard,³⁴ and there is no data on the accuracy of the 21-day surveillance strategy.

Limitations

Limitations of this review included the selected use of data sources, the moderate methodologic quality of the included studies and the heterogeneity, which prevented pooling. Although a sensitive search strategy including citation tracking was used to identify eligible studies, we did not search for grey literature (e.g., contacting key authors to identify unpublished data). The inability to pool results means that the findings of this review are based on individual studies and only one direct comparison. Factors contributing to the heterogeneity identified included between trial variations in methodologic quality, clinical characteristics (e.g., professions applying the rules, their experience and training) and within-trial variations in how rules were interpreted and applied.

Conclusion

Based on studies with modest methodologic quality, we found that both the Canadian C-spine rule and NEXUS were highly sensitive rules that have the potential to reduce imaging rates. However, the lower specificity and false-positive results indicate that many people will continue to undergo unnecessary imaging. In the only direct comparison, the Canadian C-spine rule appeared to have better diagnostic accuracy, and it should be used over NEXUS to assess the need for cervical spine imaging. Future studies of diagnostic test accuracy need to ensure that rigorous methodologic procedures are followed to reduce bias. Furthermore, the evaluation of these tools in settings outside of emergency departments, in pediatric and older populations and by primary care physicians, such as general practitioners and physiotherapists, is also required.

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