

## REVIEW ARTICLE

# Canadian C-spine Rule versus NEXUS in Screening of Clinically Important Traumatic Cervical Spine Injuries; a systematic review and meta-analysis

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**Abstract:** **Introduction:** The Canadian C-spine Rule (CCR) and the National Emergency X-Radiography Utilization Study (NEXUS) are two criteria designed to rule-out clinically important traumatic cervical Spinal Cord Injury (SCI). In this systematic review and meta-analysis, we reviewed the articles comparing the performance of these two models. **Methods:** Search was done in Medline, Embase, Scopus and Web of Science until June 2022. Observational studies with direct comparison of CCR and NEXUS criteria in detection of clinically important cervical SCI were included. Two independent reviewers screened the relevant articles and summarized the data. Certainty of evidence was assessed based on QUADAS-2. Data were recorded as true positive, true negative, false positive, and false negative. Then, using “diagma” package and applying weighted random effect model, area under the receiver operating characteristic (ROC) curve (AUC), sensitivity, specificity, negative likelihood ratio, positive likelihood ratio, and diagnostic odds ratio (DOR) were calculated with 95% confidence interval (95% CI). **Results:** We included 5 studies with direct comparison. Area under the ROC curve of NEXUS in screening of patients with clinically important cervical SCI was 0.708 (95% CI: 0.647 to 0.762). Pooled sensitivity and specificity of NEXUS criteria in screening of patients with clinically important cervical SCI were 0.899 (95% CI: 0.845 to 0.936) and 0.398 (95% CI: 0.315 to 0.488). The positive and negative likelihood ratios of NEXUS were 1.494 (95% CI: 1.146 to 1.949) and 0.254 (95% CI: 1.155 to 1.414), respectively. Diagnostic odds ratio of NEXUS was 5.894 (95% CI: 3.372 to 10.305). Furthermore, area under the ROC curve of CCR in screening of clinically important cervical SCI was 0.793 (95% CI: 0.657 to 0.884). Meta-analysis results showed that pooled sensitivity of CCR criteria in screening of patients with clinically important cervical SCI was 0.987 (95% CI: 0.957 to 0.996) and specificity was 0.167 (95% CI: 0.073 to 0.336). The positive and negative likelihood ratios of CCR were 1.184 (95% CI: 0.837 to 1.675) and 0.081 (95% CI: 0.021 to 0.308), respectively. Diagnostic odds ratio of CCR was 14.647 (95% CI: 3.678 to 58.336). **Conclusion:** Based on studies, both CCR and NEXUS were sensitive rules that have the potential to reduce unnecessary imaging in cervical spine trauma patients. However, the low specificity and false-positive results of both of these tools indicate that many people will continue to undergo unnecessary imaging after screening of cervical SCI using these tools. In this meta-analysis, CCR appeared to have better screening accuracy.

**Keywords:** Spinal cord injuries; cervical cord; wounds and injuries; diagnosis; clinical decision rules; sensitivity and specificity

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## 1. Introduction

Spinal Cord Injury (SCI) is an important concern causing severe damages to patients, both in acute and chronic phases. Based on the US National SCI statistics report, 273,000 suffer from SCI in USA (1). Although, SCI can occur in any part of the spinal cord, cervical SCI could be the most dangerous injury, causing severe life-threatening symptoms such as

impaired breathing and quadriplegia (2). An important part in the primary assessment of the patients with acute spinal injury is to rule out major pathology such as fractures (3). It is important to use a proper screening method, in order to avoid acute and chronic consequences in cervical SCI in trauma patients (4).

Imaging evaluations could help diagnose different spinal cord injuries and instabilities. However, clinically important cervical SCIs are found in only 3% of cervical trauma patients and other patients undergo unnecessary imaging and radiation exposure (4, 5). This low diagnostic yield, despite high imaging rates, is associated with significant costs and destructive effects on health system resources (6, 7). In addition, thyroid gland, as a radiosensitive tissue, is exposed to harmful radiation despite lack of proper diagnostic indication for imaging (8).

Application of rule-out criteria could help physicians diagnose clinically important cervical SCIs as well as reduce the unnecessary imaging evaluations (9). Clinical practice guidelines recommend the use of clinical decision rules to identify patients with clinically important cervical SCIs. These rules help in decision-making regarding the diagnostic and treatment process based on the findings of history and physical examination and simple diagnostic tests (10, 11).

The Canadian C-spine Rule (CCR) (12) and the National Emergency X-Radiography Utilization Study (NEXUS) (13) are two criteria designed to rule-out clinically important cervical SCIs. These tools could help in reduction of unnecessary imaging in patients with blunt trauma. CCR was first introduced in 2001 as a highly sensitive rule, applicable on alert and stable trauma patients, which could significantly reduce inefficiencies in use of C-spine radiography in emergency departments (12). NEXUS criteria to rule out injury to the cervical spine was introduced in 1998 and was defined as a reliable preliminary screening tool for cervical SCI (13). Both of these criteria have been evaluated in multiple prospective and cohort studies over the years. Currently, these criteria are recommended in guidelines as an approach to cervical spine trauma patients (14-16).

Despite their wide use, there is no consensus on superiority of any of the criteria over the other. Therefore, in this systematic review and meta-analysis we reviewed the articles comparing the performance of CCR and NEXUS in detection of clinically important cervical SCI.

## 2. Methods

### 2.1. Study design

The present study was designed to compare the accuracy of CCR and NEXUS tools in ruling out clinically important cervical SCIs in blunt trauma patients. PICO was as follows: P (patient/problem/population): human studies performed

on cervical spine trauma patients; I (index test): NEXUS and CCR decision tools; C (comparison): comparison with radiologic findings; and O (outcome): clinically important cervical SCI.

### 2.2. Participants

The study population included EMS personnel working in urban and interurban medical emergency departments in emergency medical services (EMS) affiliated to Kurdistan University of Medical Sciences, Iran. A total of 301 participants were included in the study. The inclusion criteria included willingness to participate in the study and the experience of providing care during COVID-19 pandemic in medical emergencies. The exclusion criterion was not completing the questionnaires.

### 2.3. Search strategy

In the present systematic review and meta-analysis four databases, including PubMed, Embase, Scopus, and Web of Science were searched until June 2022 the search strategy was developed based on terms describing NEXUS and CCR. The search strategy is presented in appendix 1. We performed an extra search in grey literature and in the references of the related original articles and reviews to identify the articles missed in the database searches.

### 2.4. Eligibility criteria

Randomized clinical trials (RCTs), cohorts, and cross-sectional studies on comparison of NEXUS and CCR in the same target population were included in this study. Duplicated reports, retracted papers, and review studies, as well as articles assessing only one of the mentioned criteria (indirect comparison) were excluded.

### 2.5. Data collection and risk of bias assessment

The records were imported into Endnote software (version X7; Thomson Reuters, Toronto, ON, Canada) and duplicates were eliminated. Two independent researchers selected the related articles after reviewing the title and abstract of collected records. The full texts of potentially related articles were studied in more detail. Based on the eligibility criteria, related articles were selected. Any disagreement was resolved using a third reviewer's opinion.

The data of the finally selected articles were extracted and imported into a checklist using EXCEL software. The items of the checklist consisted of article features (first author name, country, year of publication, study design), characteristics of the target population (sample size, age, gender, disease history), setting of injury, type of radiographic imaging, rule-out tools' performance (CCR or NEXUS), and risk of bias. Quality of the included studies was assessed based on QUADAS-2, which is designed to assess the quality of primary diagnostic

accuracy studies.

## 2.6. Statistical analysis

Analysis was performed using STATA 17.0 statistical software. Data were recorded as true positive, true negative, false positive, and false negative. Then, using “diagma” package and applying weighted random effect model, the area under the receiver operating characteristics (ROC) curve (AUC), sensitivity, specificity, negative likelihood ratio, positive likelihood ratio, and diagnostic odds ratio (DOR) were calculated with 95% confidence interval (95% CI). If more than 50% was defined as high heterogeneity. Deek's funnel plot asymmetry test was used to assess publication bias.

## 3. Results

### 3.1. Study characteristics

Search in databases yielded 71 nonduplicated articles. Manual search also resulted in one article. After reviewing the articles, 55 were selected, 5 of which were included in this systematic review and meta-analysis (7, 17-20). The reasons for exclusion of the selected articles were pediatric target population in the studies, lack of positive finding groups, lack of required data, non-cervical spinal trauma patients, articles evaluating only CCR or only NEXUS (indirect comparison), and articles being case-reports or reviews (figure 1). The included articles evaluated NEXUS and CCR in the same target population. All of the studies were prospective cohorts, except for one retrospective cross-sectional study. The studies included data from 14253 patients, 54.88% of whom were male. The average age range was between 34.3 to 54.6 years. All of the patients had non-penetrating cervical spine trauma. Three studies had applied plain radiography to rule out critical cervical injuries and 2 had considered computed tomography scan as the gold standard tool (Table 1). In total, 13689 patients were normal and 564 patients had traumatic cervical spinal injury.

### 3.2. Diagnostic accuracy of NEXUS Criteria

AUC of NEXUS in screening of patients with clinically important cervical SCIs was 0.708 (95% CI: 0.647 to 0.762) (Figure 2). Pooled sensitivity and specificity of NEXUS criteria in screening of patients with clinically important cervical SCIs were 0.899 (95% CI: 0.845 to 0.936) and 0.398 (95% CI: 0.315 to 0.488), respectively. The positive likelihood ratio of NEXUS was 1.494 (95% CI: 1.146 to 1.949) and its negative likelihood ratio was 0.254 (95% CI: 1.155 to 1.414). Diagnostic odds ratio of NEXUS was 5.894 (95% CI: 3.372 to 10.305) (Table 2).

### 3.3. Diagnostic accuracy of CCR Criteria

AUC of CCR in screening of patients with clinically important cervical SCIs was 0.793 (95% CI: 0.657 to 0.884) (Figure 2).

Meta-analysis results showed that, pooled sensitivity of CCR criteria in screening of patients with clinically important cervical SCIs was 0.987 (95% CI: 0.957 to 0.996) and its specificity was 0.167 (95% CI: 0.073 to 0.336). The positive likelihood ratio of this test was 1.184 (95% CI: 0.837 to 1.675) and its negative likelihood ratio was 0.081 (95% CI: 0.021 to 0.308). Diagnostic odds ratio of CCR was 14.647 (95% CI: 3.678 to 58.336) (Table 2).

### 3.4. Risk of Bias Assessment

In the patient selection item, one study was rated as high-risk in both risk of bias and applicability domains. The other four articles had a low risk in patient selection item. In the field of index test, there were two studies with a high risk of bias, one of which was also high-risk in applicability item. All studies were low-risk in reference tests. One study had an unclear risk in flow and timing domain and one was high-risk in this field. Overall, two studies had some concern and other three studies were low-risk studies (Table 3).

### 3.5. Publication bias

Egger's test showed no evidence of publication bias among the studies. As shown in funnel plot (Figures 2 and 3) no plot asymmetry was observed for NEXUS ( $p=0.32$ ) and CCR ( $p=0.87$ ) criteria.

## 4. Discussion

Using imaging as a screening tool to rule out cervical spine injuries in blunt trauma patients is not cost-beneficial. It also exposes patients to unnecessary radiation. Therefore, physicians use decision rules for screening blunt trauma patients with cervical spine injuries. The two most common decision rules used in diagnosing cervical spine injuries in blunt trauma patients are CCR and NEXUS (21).

In the current systematic review, five studies that had evaluated the diagnostic accuracy of CCR and NEXUS criteria in detection of patients with clinically important cervical SCIs were included. It seems that CCR has a higher sensitivity, negative likelihood ratio, and diagnostic odds ratio in detection of cervical spine injuries compared to NEXUS. In other words, CCR is a convenient tool for determining the need for imaging and finding critical neck trauma cases.

The results of our study are consistent with the previous meta-analysis in this field. Similar to the findings of the present study, the previous systematic review and meta-analysis concluded that CCR has higher sensitivity than NEXUS(22). However, our study has an advantage, since we enrolled only the papers evaluating the effectiveness of NEXUS and CCR on the same population. In other words, these studies have conducted a direct comparison. The last meta-analysis in this field was conducted in 2012 by Michal-

**Table 1:** Study characteristics

Author, Year	Country	Study design	Study type	Sample Size	Age (year)	Male	Reference Test	Time to Reference Test	N CSI	N Normal	Rule	Sensitivity	Specificity
Ala, 2018	Iran	Prospective	Cohort	200	40.0 ± 17.7	139	X-Ray	NR	10	190	NEXUS	90	44.2
											CCR	90	54.73
Benayoun, 2016	USA	Retrospective	Cross-sectional	760	53.6	483	CT	NR	7	753	NEXUS	100	29.8
											CCR	100	24
Duane, 2013	USA	Prospective	Cohort	5182	NR	NR	CT	24 hr	324	4858	NEXUS	100	0.62
											CCR	81.17	45.8
Ghelichkhani, 2021	Iran	Prospective	Cohort	673	34.3 ± 19.4	466	X-Ray	NR	61	612	NEXUS	100	8.3
											CCR	93.4	52.3
Stiell, 2003	Canada	Prospective	Cohort	7438	37.6 ± 16.0	3890	X-Ray	NR	162	7276	NEXUS	99.4	45.1
											CCR	90.7	36.8

CSI: cervical spine injury; CT: computed tomography scan; NR: Not reported; NEXUS: national emergency X-radiography Utilization study; CCR: Canadian C-spine rule.

**Table 2:** Screening performance characteristics of NEXUS and CCR criteria in detection of patients with clinically important cervical spinal cord injuries

Characteristics	Value (95%CI)
<b>National emergency X-radiography Utilization study (NEXUS)</b>	
Area under the ROC curve	0.708 (0.647, 0.762)
Sensitivity	0.899 (0.845, 0.936)
Specificity	0.398 (0.315, 0.488)
Positive likelihood ratio	1.494 (1.146, 1.949)
Negative likelihood ratio	0.254 (0.155, 0.414)
Diagnostic odds ratio	5.894 (3.372, 10.305)
<b>Canadian C-spine rule (CCR)</b>	
Area under the ROC curve	0.793 (0.657, 0.884)
Sensitivity	0.987 (0.957, 0.996)
Specificity	0.167 (0.073, 0.336)
Positive likelihood ratio	1.184 (0.837, 1.675)
Negative likelihood ratio	0.081 (0.021, 0.308)
Diagnostic odds ratio	14.647 (3.678, 58.336)

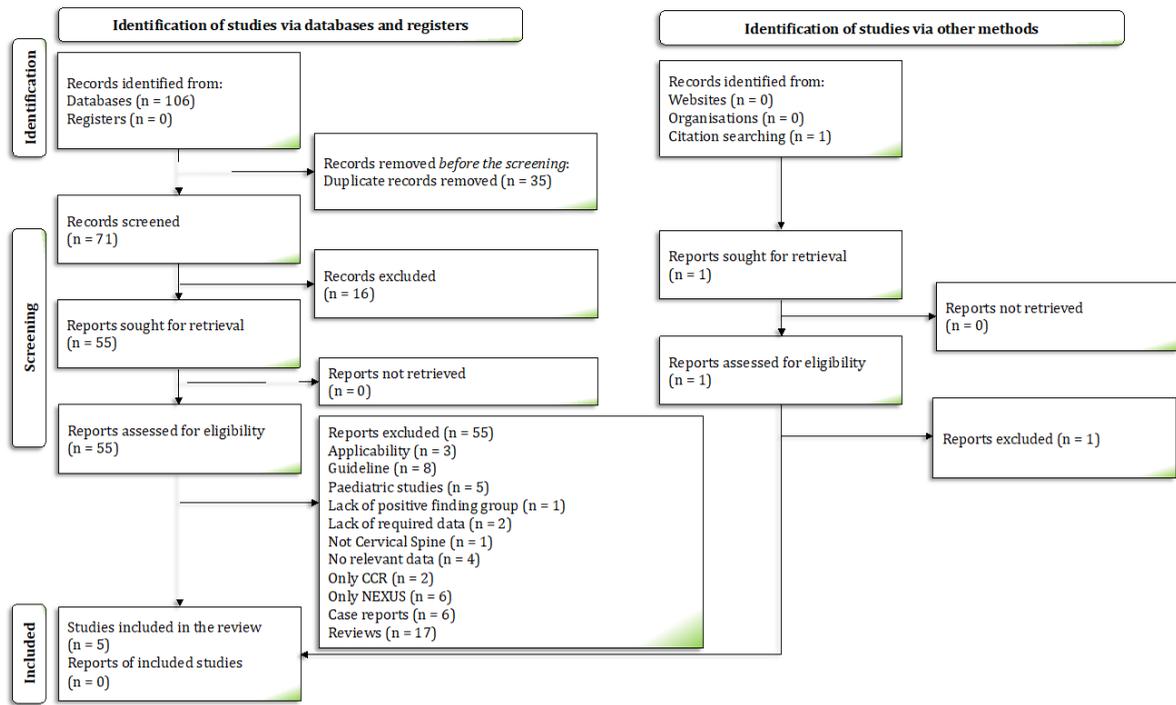
CI: confidence interval; ROC: receiver operating characteristic.

**Table 3:** Risk of Bias assessment of included studies

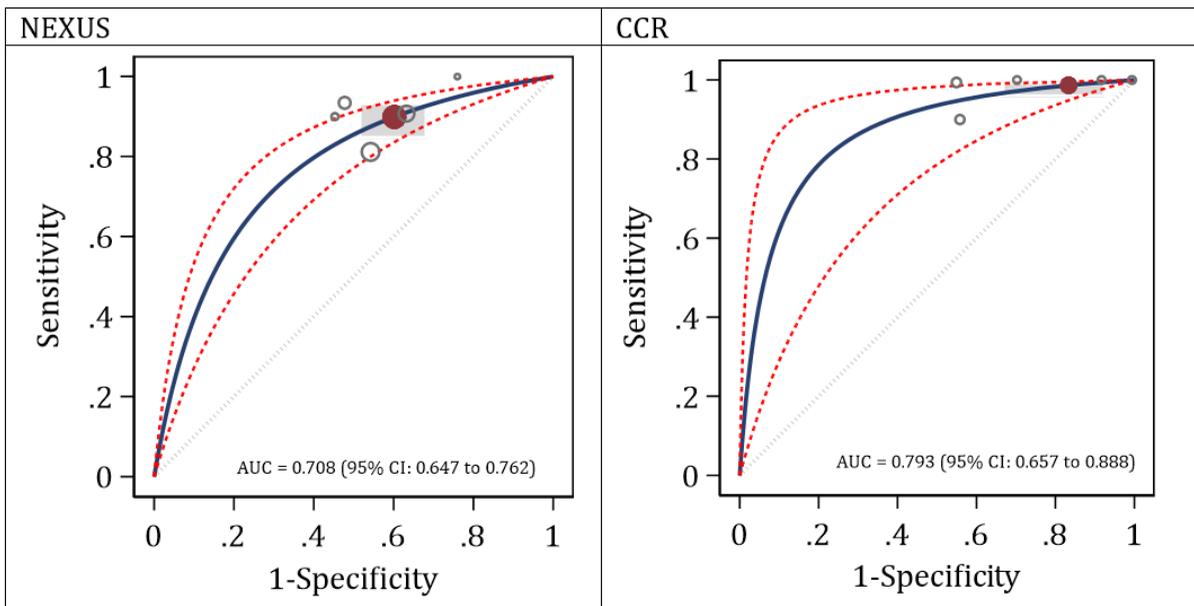
Author, Year	Risk of Bias				Applicability			overall
	Patient selection	Index test	Reference test	Flow and timing	Patient selection	Index test	Reference test	
Ala, 2018	Low	Low	Low	Unclear	Low	Low	Low	Low
Benayoun, 2016	High	High	Low	High	High	Low	Low	Some concern
Duane, 2013	Low	High	Low	Low	Low	High	Low	Some concern
Ghelichkhani, 2021	Low	Low	Low	Low	Low	Low	Low	Low
Stiell, 2003	Low	Low	Low	Low	Low	Low	Low	Low

eff et al. (22). In this paper only one study had direct comparison. It has been a decade since that article was published, and only four additional articles have been published,

directly comparing CCR and NEXUS. There is a need for well-designed cohort studies in this field in order to reach more reliable results.



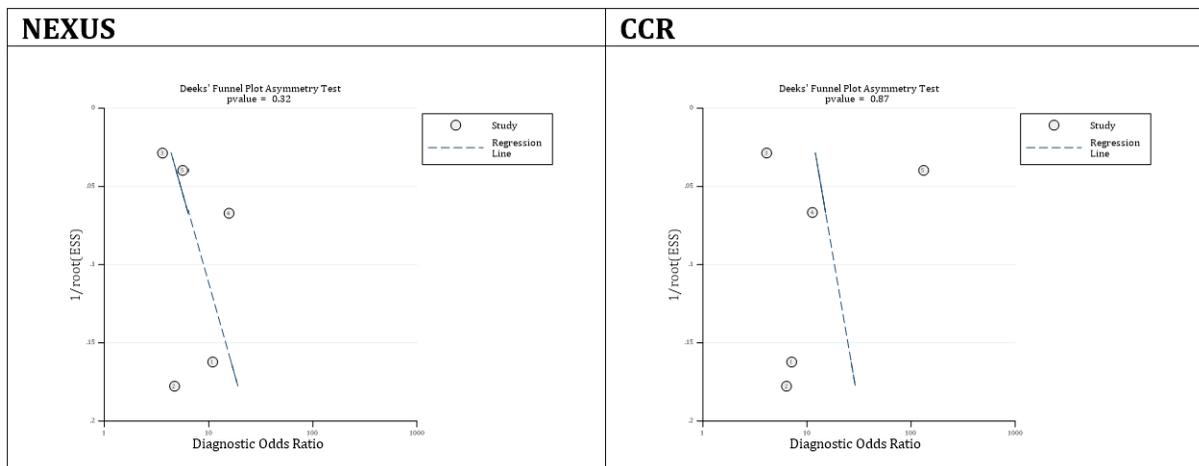
**Figure 1:** PRISMA flowchart of included studies. NEXUS: national emergency X-radiography Utilization study; CCR: Canadian C-spine rule.



**Figure 2:** Area under the receiver operating characteristic curve (AUC) of National Emergency X-Radiography Utilization Study (NEXUS) and Canadian Cervical Spine Rule (CCR) in detection of patients with clinically important cervical spinal cord injuries.

Both of these screening tools had a sensitivity of almost ninety percent. A high sensitivity in these tools was reported

in the previous studies as well (23, 24). Based on the age of the patients, the results may vary in studies. For instance, it has



**Figure 3:** Funnel plot for assessment of publication bias regarding diagnostic accuracy of National Emergency X-Radiography Utilization Study (NEXUS) and Canadian Cervical Spine Rule (CCR).

been shown that, the sensitivity of NEXUS criteria decreases in older patients (23).

It seems that CCR is not capable of reducing the unnecessary imaging among the geriatric cervical blunt trauma patients, because of high false positive rates. However more studies are required to prove this finding (21). Therefore, despite the advantage of CCR in the screening of cervical spine injuries in blunt trauma patients, it could not yet replace NEXUS in geriatric age group.

## 5. Limitation

Limitations of this review included the moderate methodological quality of the included studies and the heterogeneity among the studies. There are more studies evaluating the efficacy of NEXUS and CCR, separately. However, only five studies compared both these rules simultaneously, on the same target population. More well-designed studies are needed, in order to achieve a more reliable conclusion in this field. Moreover, there was some concern regarding the risk of bias of two studies, which highlights the necessity of more well-designed studies.

## 6. Conclusion

We found that both CCR and NEXUS were sensitive rules that have the potential to reduce unnecessary imaging in cervical spine trauma patients. However, the low specificity and false-positive results of both of these tools indicate that many people will continue to undergo unnecessary imaging after screening of cervical SCI using these tools. In this meta-analysis, the CCR rule appeared to have better screening accuracy.

## 7. Declarations

### 7.1. Acknowledgments

None.

### 7.2. Conflict of interest

There is no conflict of interest.

### 7.3. Fundings and supports

None.

### 7.4. Authors' contribution

All authors have same contribution in all steps of the current study.

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**Appendix 1:** Risk of Bias assessment of included studies

<b>Search strategy</b>
<b>Medline (PubMed)</b>
(Canadian C-Spine[tiab] OR low risk cervical spine criteria[tiab]) AND (National Emergency X-Radiography Utilization Study[tiab] OR NEXUS[tiab] OR low risk cervical spine criteria[tiab])
<b>Embase</b>
1- 'National Emergency X-Radiography Utilization Study':ab,ti OR 'NEXUS':ab,ti OR 'low risk cervical spine criteria':ab,ti 2- 'canadian c spine rule'/exp OR 'Canadian C-Spine':ab,ti OR 'low risk cervical spine criteria':ab,ti 3- #1 AND #2
<b>Scopus</b>
1- TITLE-ABS-KEY("National Emergency X-Radiography Utilization Study" OR "NEXUS" OR "low risk cervical spine criteria") 2- TITLE-ABS-KEY("Canadian C-Spine" OR "low risk cervical spine criteria") 3- #1 AND #2
<b>Web of Science</b>
1- TS=("National Emergency X-Radiography Utilization Study" OR "NEXUS" OR "low risk cervical spine criteria") 2- TS=( "Canadian C-Spine" OR "low risk cervical spine criteria") 3- #1 AND #2