PEDIATRIC EMERGENCY MEDICINE CRITICAL ARTICLE REVIEW (PEMCAR)	
QUESTION	In children less than 18 years of age who sustain blunt trauma are clinical signs and symptoms accurate in identifying those a low risk for cervical spine injury who could potentially forgo cervical spine imaging?
TYPE	Diagnosis: Clinical Decision Rule: Derivation and Validation
TOPIC	Trauma: Cervical Spine Injury
DATE	July 2019
REVIEWER	Michael Mojica, MD
CITATION	Leonard JC, Browne LR, Ahmad FA, Schwartz H, Wallendorf M, Leonard JR, Lerner EB, Kuppermann N. Cervical Spine Injury Risk Factors in Children with Blunt Trauma. Pediatrics. 2019 Jul;144(1)., PubMed ID: 31221898

STUDY DEFINITIONS	
POPULATION	Inclusion: < 18 years with blunt trauma Transported from the scene by EMS Present to the ED either directly via EMS or in transfer Underwent a trauma evaluation with or without cervical spine imaging Exclusion: Penetrating trauma Legal guardian with a significant English language barrier Transferred from the study site for definite care Setting: n=3 Level I trauma Children's Hospitals (U.S.), 3/2014-11/2016
RULE PARAMETERS	Factors with biologic or anatomic plausibility and good inter-rater reliability. Included: Mechanism of injury/injury biomechanics variables and patient history, signs and symptoms variables (See Appendix: Candidate variables)
REFERENCE STANDARD	Cervical Spine Injury: Occiput to C7 Vertebral fracture Ligamentous injury (including ligaments attached to T1) Intraspinal hemorrhage Spinal cord injury: MRI or spinal cord injury without radiographic abnormality ED imaging performed: Review of c-spine imaging reports and spine surgeon consultation notes if applicable No ED imaging performed: Medical record review at 28 days for subsequent imaging. If no imaging obtained then phone follow up at 21-28 days after ED visit
OUTCOME	Rule characteristics, potential reduction in XRAY utilization
DESIGN	Observational: Prospective cohort

CRITICAL REVIEW FORM: CLINICAL DECISION RULE: DERIVATION

HOW SERIOUS WAS THE RISK OF BIAS?	
Were all important predictors included in the derivation process?	Yes. An extensive list of candidate factors with biologic or anatomic plausibility and good inter-rater reliability were included in the derivation process (See Appendix: Candidate variables).

Were all important predictors present in significant proportion of the study population?	Unclear. The proportion of patients with the significant predictors was not presented. The authers only note that predisposing conditions occurred in < 1 % of patients.
Were the outcome event and predictors clearly defined?	Yes. The outcome of cervical spine injury was clearly defined as an injury from the occiput to C7 (including ligamentous attachments to T1) involving the vertebra, ligaments, extraspinal space (hemorrhage) and spinal cord.
Were those assessing the outcome event blinded to the presence of the predictors and were those assessing the presence of predictors blinded to the outcome event?	Yes. Data was collected prior to the results of imaging. For transfer patients, data was collected prior to imaging interpretation by the radiologist at the study institution but clinicians may have been aware of imaging results from the transferring institution. 42% (31/74) of those with cervical spine injury were transfers. However, when a subgroup analysis that excluded transfer patients was conducted, the test characteristics for both models remained similar.
Was the sample size adequate (including an adequate number of outcome events)?	In general, a sample size of 10 outcomes per variable in the model is considered adequate for logistic regression. 74 patients with cervical spine injury were included. 9 variables were included in the PECARN model (6 were statistically significant). 7 variables were included in de novo model.

WHAT ARE THE RESULTS?

HOW WELL DID THE RULE CORRECTLY IDENTIFY PATIENTS WITH THE PRIMARY OUTCOME? HOW PRECISE WAS THIS MEASUREMENT? (SENSITIVITY AND PREDICTIVE VALUE OF A NEGATIVE RULE WITH 95% CONFIDENCE INTERVALS)

HOW WELL DID THE RULE CORRECTLY IDENTIFY PATIENTS WITHOUT THE PRIMARY OUTCOME? HOW PRECISE WAS THIS MEASUREMENT? (SPECIFICITY AND PREDICTIVE VALUE OF A POSITIVE RULE WITH 95% CONFIDENCE INTERVALS)

Cervical Spine Injury: 1.8% (74/4,091)
Mean age: 9.4 years (all patients), 10.7 years (patients with CSI)
Age < 8 years, 39.3% (1,608/4,091), CSI: 1.4% (23/1,608), 31.1% of those with CSI: (23/74)
Non-transfer patients: 76.7% (3,138/4,091), CSI: 1.4% (43/3,138)
Imaging obtained: 78.2%

INDEPENDENT PREDICTORS OF CSI: REGRESSION ANALYSIS

PREDICTOR	PECARN MODEL[1]	DE NOVO MODEL[1]
Mechanism: High Risk MVC	1.58 (0.63, 3.97)	
Mechanism: Diving	17.60 (5.60, 55.32)	9.16 (2.41, 34.83)
Mechanism: Axial Load		2.51 (1.22, 5.16)
History: Predisposing Condition	2.02 (0.27, 15.10)	
History: Neck Pain[2]	1.65 (1.04, 2.62)	2.87 (1.50, 5.48
History: Inability to Move Neck[2]	3.77 (2.00, 7.12)	3.51 (1.72, 7.17)
Exam: Altered Mental Status	5.67 (3.54, 9.09)	2.90 (1.37, 6.12)
Exam: Intubated		10.71 (4.43, 25.91)
Exam: Limited Neck Range of Motion	1.85 (0.88, 3.90)	
Exam: Substantial Torso Injury	2.61 (1.24, 5.53)	
Exam: Respiratory Distress		5.84 (1.56, 21.88)
Exam: Focal Neurologic Deficits	2.62 (1.04, 6.63)	

GREEN = Statistically Significant, RED = Not Statistically Significant
1. Adjusted Odds Ratio (95% Confidence Interval)
2. Neck pain and inability to move neck were assessed separately. These were combined as Torticollis in the derivation of the original PECARN case-control study

TEST CHARACTERISTICS

PECARN RULE		CSI		
		Yes	No	
≥ 1 Factor[1]	Yes	67	2,186	2,253
	No	7	1,831	1,838
		74	4,017	4,091
Sensitivity		90.54% (83.87, 97.21%)		
Specificity		45.58% (44.04, 47.12%)		
PV (+) Test		2.97% (2.27, 3.68%)		
PV (-) Test		99.62% (99.34, 99.90%)		
LR (+) Test		1.66 (1.54, 1.80)		
LR (-) Test		0.21 (0.10, 0.42)		

DE NOVO RULE		CSI		
		Yes	No	
≥ 1 Factor	Yes	68	1,998	2,066
	No	6	2,019	2,025
		74	4,017	4,091
Sensitivity		91.88% (85.7, 98.11%)		
Specificity		50.26% (48.72, 51.81%)		
PV (+) Test		3.29% (2.52. 4.06%)		
PV (-) Test		99.71% (99.47, 99.94%)		
LR (+) Test		1.85 (1.71, 1.99)		
LR (-) Test		0.16 (0.07, 0.35)		

1. Any of the 9 factors in the PECARN rule including the 3 that were not statistically significant

SUBGROUP ANALYSIS (WITH/WITHOUT TRANSFER PATIENTS)

		SENSITIVITY	SPECIFICITY
PECARN Model	All Patients	90.5% (83.9, 97.2%)	45.6% (44.0, 47.1%)
	Transfers Excluded	93.0% (85.4, 100%)	42.1% (40.3, 43.8%)
De Novo Model	All Patients	91.9% (85.7, 98.1%)	50.26% (48.7, 51.8%)
	Transfers Excluded	95.3% (89.1, 100%)	45.9% (44.1, 47.7%)

HOW WOULD USE OF THE RULE IMPACT RESOURCE UTILIZATION?

Utilizing the PECARN rule, 44.9% (1,838/4,091) of patients did not have any risk factors and could potentially forgo imaging. Alternatively, 55.1% would have imaging if those with at least 1 factor underwent imaging.

Utilizing the De Novo rule 49.4% (2,024/4,091) of patients did not have any risk factors and could potentially forgo imaging. Alternatively, 51.6% would have imaging if those with at least 1 factor underwent imaging.

The potential decrease in imaging would depend on the baseline rate of imaging. The authors extrapolated a decrease in the rate of imaging from a baseline rate of 78.2%. Imaging wound potential be reduced by 22.1% (78.2% - 55.1%) for the PECARN rule and by 26.6% (78.2% - 51.6%) for the De Novo rule.

WAS THERE AN INTERNAL STATISTICAL VALIDATION OF THE RESULTS? HOW DID IT COMPARE TO THE PRIMARY RESULTS?

Interval validation of the rule was not presented. The original PECARN derivation study had a higher sensitivity of 98%, 95% CI (96, 99%) and a lower specificity of 26%, 95% CI (23, 29%).

HOW CAN I APPLY THE RESULTS TO PATIENT CARE?

At what level of development is this rule? How can it be applied? (See Appendix)	☐ I ☐ II ☐ III ■ IV The de novo rule is level IV rule. The PECARN rule is also a level IV rule (a re-derivation with different predictors). A level IV rule has been derived only or

	validated only in split samples, large retrospective databases or by statistical methods. A level IV rule requires further validation before it can be applied clinically.
Does the rule make clinical sense?	Yes. The factors in both of the rules assess factors that are associated with cervical spine injury. However, a distracting injury which is a factor in the NEXUS criteria was not assessed as a candidate variable though it is the most subjective of the NEXUS criteria.
Will the reproducibility of the rule and its interpretation be satisfactory in my clinical setting?	Unclear. The authors included factors with biologic or anatomic plausibility and good inter-rater reliability. The kappa statistics for the significant predictors were not presented.
Is the rule applicable to the patients in my practice?	Yes. We evaluate pediatric trauma patients with a potential for cervical spine injury. However, motor vehicle collision was the most common mechanism of injury in the study and pedestrians struck by motor vehicles is a more common mechanism in NYC. It is unclear if these mechanisms result in different patterns of injury.
Will the rule results change my management strategy?	Unlikely. These are the parameters that we currently use to assess the risk of c-spine injury. I would wait for the follow up study in the entire PECARN network to validate the two models. Only 74 patients with c-spine injury were included in the analysis (n=23 in those less than 8 years of age).
What are the benefits of applying the rule to my patients?	The primary benefit of using either of the decision rules is a reduction in imaging. Pediatric plain films are often difficult to obtain and interpret. CT scan is associated with radiation exposure. The authors extrapolated a decrease in the rate of imaging from a baseline rate of 78.2%. Imaging wound potential be reduced by 22.1% (78.2% - 55.1%) for the PECARN rule and by 26.6% (78.2% - 51.6%) for the De Novo rule.
What are the risks of applying the rule to my patients?	The primary risk of applying either of the decision rules is in missing patients with a cervical spine injury. The PECARN rule missed 9.5% (7/74) of those with cervical spine injury. The de novo rule missed 8.1% (6/74) of those with cervical spine injury. 6 of the patients missed did not require surgical intervention. Treatment of the 7th patient is unknown. 1 missed patient required a brace and another required a hard, cervical collar (Table 5).

CLINICAL BOTTOM LINE

BACKGROUND: Pediatric cervical spine injuries are rare (< 1% after blunt trauma). Decision rules to identify risk of cervical spine injury in adults have been developed (NEXUS criteria, Canadian C-spine rule). A pediatric rule was developed as a subset of the Nexus study. (Vicellio, Pediatrics 2001, PubMed ID: 11483830). The pediatric NEXUS included only 30 patients with cervical spine injuries. While the sensitivity of the rule was 100%, the lower limit of the 95% confidence interval was 88% due to the small sample size.

The PECARN group previously conducted a case-control study to derive a pediatric cervical spine clinical decision rule (Leonard, Ann Emerg Med. 2011, PubMed ID: 21035905). The study identified 8 predictors of pediatric cervical spine injury. These included 1 history parameter (predisposing conditions), 2 mechanism of injury parameters (diving, high risk motor vehicle collision), 1 symptom parameter (complaint of neck pain) and 4 physical examination parameters (focal neurologic deficit, altered mental status, substantial torso injury, torticollis). The rule performed with a sensitivity of 98% 95% CI (96, 99%) and specificity of 26% 95% CI (23, 29%) for cervical spine injury. The sensitivity for identifying cervical spine injury requiring neurosurgical intervention using all sources of data was 98%, 95% CI (95, 99%). To date, the rule has not been validated.

CLINICAL QUESTION: In children less than 18 years of age who sustain blunt trauma are clinical Signs and symptoms accurate in identifying those a low risk for cervical spine injury who could potentially forgo cervical spine imaging?

DESIGN/RISK OF BIAS: This was a well-designed prospective cohort study conducted at 4 children's hospitals that are level I trauma centers. Patients less than 18 years with blunt trauma who were transported from the scene by emergency medical services to the ED either directly or in transfer from another institution and who underwent a trauma evaluation with or without cervical spine imaging were included. Patients with penetrating trauma, a legal guardian with a significant English language barrier and those who were transferred from the study site for definite care were excluded.

Candidate predictors were those with biologic or anatomic plausibility and good inter-rater reliability. These included mechanism of injury/injury biomechanics variables and patient history, signs and symptoms variables (See Appendix: Candidate Variable). The outcome of cervical spine injury was clearly defined as an injury from the occiput to C7 (including ligamentous attachments to T1) involving the vertebra, ligaments, extraspinal space (hemorrhage) and spinal cord. The outcome was assessed by review of c-spine imaging reports and spine surgeon consultation notes if applicable for those that had imaging. The outcome was assessed by medical record review at 28 days to determine is subsequent imaging was obtained. If no subsequent imaging was obtained then phone follow-up occurred at 21-28 days after ED visit.

It is somewhat unusual to include transfer patients as knowledge of the reason for transfer including imaging results may bias interpretation of the predictor variables. For transfer patients, data was collected prior to imaging interpretation by the radiologist at the study institution but clinicians may have been aware of imaging results at the transferring institution. 42% (31/74) of those with cervical spine injury were transfers. However, when a subgroup analysis that excluded transfer was conducted, the test characteristics for both models remained similar

In addition, the proportion of patients with the significant predictors was not presented.

PRIMARY RESULTS: Cervical spine injury occurred in 1.8% (74/4,091). 39.3% of the patients were less than 8 years of age. These patients had a cervical spine injury rate of 1.4% (23/1,608) 23.3% of the patients were transferred and imaging was obtained in 78.2% of patients.

7 independent predictors of cervical spine injury were identified in the de novo model. In the

PECARN model 3 of the 9 predictors identified in the derivation were not statistically significantly associated with cervical spine injury in the regression analysis. These were high risk motor vehicle collision, predisposing medical condition and limited neck range of motion on examination. Four factors were common to both rules. These include: a mechanism of diving, a history of neck pain, a history of inability to move the neck and physical examination consistent with altered mental status. Of note, neck pain and inability to move neck were assessed separately (these were combined in the original PECARN derivation as torticollis).

INDEPENDENT PREDICTORS OF CSI: REGRESSION ANALYSIS		
PREDICTOR	PECARN MODEL[1]	DE NOVO MODEL[1]
Mechanism: High Risk MVC	1.58 (0.63, 3.97)	
Mechanism: Diving	17.60 (5.60, 55.32)	9.16 (2.41, 34.83)
Mechanism: Axial Load		2.51 (1.22, 5.16)
History: Predisposing Condition	2.02 (0.27, 15.10)	
History: Neck Pain[2]	1.65 (1.04, 2.62)	2.87 (1.50, 5.48
History: Inability to Move Neck[2]	3.77 (2.00, 7.12)	3.51 (1.72, 7.17)
Exam: Altered Mental Status	5.67 (3.54, 9.09)	2.90 (1.37, 6.12)
Exam: Intubated		10.71 (4.43, 25.91)
Exam: Limited Neck Range of Motion	1.85 (0.88, 3.90)	
Exam: Substantial Torso Injury	2.61 (1.24, 5.53)	
Exam: Respiratory Distress		5.84 (1.56, 21.88)
Exam: Focal Neurologic Deficits	2.62 (1.04, 6.63)	

GREEN = Statistically Significant, RED = Not Statistically Significant

1. Adjusted Odds Ratio (95% Confidence Interval)
2. Neck pain and inability to move neck were assessed separately. These were combined in the original PECARN derivation as Torticollis

Test characteristics were slightly better for the de novo rule than for the PECARN rule. However, a statistical comparison of the test characteristics was not presented. Test characteristics did not differ appreciably in a subgroup analysis that excluded transfer patients.

The de novo rule divided a group with 1.8% cervical spine injury into a low risk group if there were no risk factors (1-PV(-) = 0.3%) and a high risk group (PV(+) = 3.3% if at least 1 factor was present.

The PECARN rule divided a group with 1.8% cervical spine injury into a low risk group if there were no risk factors (1-PV(-) = 0.3%) and a high risk group (PV(+) = 3.0% if at least 1 factor was present. The original PECARN derivation study had a higher sensitivity of 98%, 95% CI (96, 99%) but a lower specificity of 26%, 95% CI (23, 29%).

RULE CHARACTERISTICS									
PECARN RULE		CSI			DE NOVO RULE		CSI		
		Yes	No				Yes	No	
≥ 1 Factor[1]	Yes	67	2,186	2,253	≥ 1 Factor	Yes	68	1,998	2,066
	No	7	1,831	1,838		No	6	2,019	2,025
		74	4,017	4,091			74	4,017	4,091
Sensitivity		90.54% (83.87, 97.21%)			Sensitivity		91.88% (85.7, 98.11%)		
Specificity		45.58% (44.04, 47.12%)			Specificity		50.26% (48.72, 51.81%)		
PV (+) Test		2.97% (2.27, 3.68%)			PV (+) Test		3.29% (2.52. 4.06%)		
PV (-) Test		99.62% (99.34, 99.90%)			PV (-) Test		99.71% (99.47, 99.94%)		

LR (+) Test	1.66 (1.54, 1.80)	LR (+) Test	1.85 (1.71, 1.99)
LR (-) Test	0.21 (0.10, 0.42)	LR (-) Test	0.16 (0.07, 0.35)
1. Any of the 9 factors in the PECARN rule including the 3 that were not statistically significant			

APPLICABILITY: The inclusion of transfer patients in the study likely makes the study's results generalizable to patients meeting the study's inclusion and exclusion criteria.

The de novo rule is level IV rule. The PECARN rule is also a level IV rule (a re-derivation with different predictors). A level IV rule has been derived only or validated only in split samples, large retrospective databases or by statistical methods. A level IV rule requires further validation before it can be applied clinically.

AUTHOR'S CONCLUSION: "In this prospective cohort of children with blunt trauma, we confirmed that there are risk factors with good test accuracy in identifying cervical spine injury. We also demonstrated that incorporating these risk factors into a clinical prediction rule has the potential to substantially reduce cervical spine imaging during trauma evaluation of children. A future, adequately powered prospective observational study aimed at using these risk factors to construct a definitive pediatric cervical spine injury prediction rule is warranted."

POTENTIAL IMPACT: This is a pilot study in one of the PECARN network nodes that will be further investigated in the larger PECARN network. The study demonstrated the use of the rule could potentially decrease imaging usage by 20-25% at the expense of rarely missing patients with cervical spine injury ((8-10% of those with CSI were not identified by the rules). None of the missed patients required a surgical intervention. The small number of patients with c-spine injury (n=74) (n=23 in those less than 8 years of age) results in wide confidence intervals.

The authors conclude that further study is required before implementation of either rule. I would recommend waiting for the follow-up study in the entire PECARN network to validate the two models before changing clinical practice.

APPENDIX: CANDIDATE VARIABLES

CANDIDATE VARIABLES
MECHANISM OF INJURY AND INJURY BIOMECHANICS
High risk motor vehicle collision
Compartment intrusion: Roof > 12 inches at passenger site or > 18 inches at any site
Partial of complete ejection from the vehicle
Death of a passenger in the same compartment
Vehicle telemetry consistent with high-risk crashes
Diving, axial load of clotheslining
Force caused by a rope, cable or other similar exerting traction on neck while body moving forward
PATIENT HISTORY VARIABLES
Predisposing conditions
Loss of consciousness
Neck pain
Inability to move neck
Paresthesias
Numbness
Weakness
PHYSICAL EXAMINATION FINDINGS
Altered mental status
Intubation
Signs of substantial head injury other than altered mental status
Signs of basilar skull fracture
Posterior midline neck tenderness to palpation
Limited range of neck motion
Substantial* torso injury
Substantial* thorax injury
Substantial* abdominal injury
Substantial* pelvic injury
Decreased oxygen saturation
Thoracic spine tenderness
Lumbar spine tenderness
Sacral spine tenderness
Focal neurologic deficits: Paresthesia, decreased sensation, weakness
*Substantial injury: Life threatening and warranting surgical intervention OR warranting inpatient observation

APPENDIX: CLINICAL DECISION RULE STAGES

LEVEL	CRITERIA	APPLICABILITY
I	• ≥ 1 prospective validation in population separate from derivation set • Impact analysis with change in clinician behavior and benefit	Use rule in wide variety of settings with confidence
II	• Validated in 1 large prospective study including a broad spectrum of patients or in several smaller settings that differ from each other. • No impact analysis	Use rule in wide variety of settings with confidence in the accuracy of the rule but no certainty that patient outcomes will improve
III	• Validated in 1 narrow prospective sample	Consider use with caution and only in patients similar to the study population
IV	• Rule has been derived only or validated only in split samples, large retrospective databases or by statistical methods	Requires further validation before it can be applied clinically