

Pediatric Emergency Care Applied Research Network (PECARN)

**Predicting Cervical Spine Injury (CSI) in Children:
A Multi-Centered Case-Control Analysis Version 9/1/2006**

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Abstract

Cervical spine injuries (CSI) are serious, but rare events in children. Immobilization of children with CSI in the out-of-hospital setting may be beneficial, but is poorly studied. In contrast, immobilization for transport of pediatric trauma patients without CSI is common and known to be associated with adverse effects. As a result, more than 99% of immobilized children have no CSI and are exposed to harm with no demonstrable benefit.

The purpose of this study is to identify a set of variables that separate injured children with negligible risk of CSI from those at non-negligible risk for CSI. To achieve our purpose, we have established two specific goals: To describe CSI and to identify factors associated with increased risk for CSI among a diverse pediatric blunt trauma population.

This work will be conducted within the Pediatric Emergency Care Applied Research Network (PECARN), a multi-centered, collaborative pediatric emergency medicine research network. We will conduct a retrospective case-control study to include 550 children with CSI. We will identify clinical and mechanism-of-injury factors that occur at high frequency among children with CSI. We will report the proportion of children with CSI who meet the National Emergency X-ray Utilization Study (NEXUS) screening criteria for CSI among adults. We will create three control groups for comparison: (1) unmatched, (2) matched for age and mechanism of injury, and (3) age matched group of children who were transported to hospital by EMS. This control group will be compared to cases of CSI who were similarly transported. These comparison groups will allow us to identify independent risk factors for CSI that will be highly sensitive in predicting non-negligible risk of CSI in children.

Analysis of the cases will be conducted for the entire study sample and for clinically relevant sub-samples. We will report all descriptive statistics, and the proportion of patients who satisfy one or more of the NEXUS screening criteria for CSI. We will compare sub-samples using chi-square analysis and t-tests. For each control group, we will report descriptive statistics. For each case-control comparison, we will report CSI odds ratios with 95% confidence intervals for independent variables. We will conduct a multivariate conditional logistic regression to determine the association of the demographic characteristics, mechanisms of injury, and clinical presentation variables with CSI. To determine the fit of the regression model, we will calculate standard goodness-of-fit statistics and receiver-operator characteristic (ROC) curves of various models. This will identify variables that have the greatest ability to distinguish between patients with and without CSI.

This study utilizes the PECARN network to produce the largest case control study of pediatric CSI ever reported. We expect the risk screening variables derived from this study to prove valuable in developing new field management strategies that will limit spinal immobilization and its adverse consequences to those at non-negligible risk for CSI.

Introduction

Cervical spine injuries (CSI) are serious, but rare events in children.^{1,2} Immobilization of children with CSI in the out-of-hospital setting may be beneficial, but is poorly studied.^{3,4,5,6,7,8} In contrast, immobilization for transport of pediatric trauma patients without CSI is common and known to be associated with adverse effects.⁹⁻²³ As a result, more than 99% of immobilized children have no CSI and are exposed to harm with no demonstrable benefit. There is a need to develop a set of CSI screening criteria that can be applied in the field to reduce the number of children who are immobilized unnecessarily while providing immobilization to those who are truly at risk for CSI.⁵

Improving the field of triage and management of injured children, especially those with central nervous system injury, has been identified as high priority for research in EMSC.⁶ The EMSC research agenda listed management of major clinical entities, prevention and relief of physical and emotional pain, and evaluation of effect and costs of out-of-hospital EMS interventions as high priorities.⁷ The EMSOP report on EMS outcomes listed trauma as the highest priority for children and specifically mentioned that relief of discomfort was the most important outcome for minor trauma.⁸

Literature Review

Historically, full spinal immobilization has been recommended for all trauma patients meeting criteria for transport to a trauma center with the belief that maintaining the spine in a neutral position and minimizing spine motion during transport will limit neurological injury.³ Recently, this practice has been disputed. Evidence has emerged that challenges the efficacy of spinal immobilization in providing neutral positioning and in limiting neurological injury for those patients with CSI. A recent retrospective analysis among adults with CSI suggests that immobilization may worsen neurological outcomes.⁴ Studies evaluating spine positioning during immobilization indicate that patients, depending on habitus, are often immobilized in non-physiologic positions. In children younger than eight years, full spinal immobilization without shoulder padding results in cervical kyphosis due to a relatively large head.^{9,10} Spinal immobilization in adults, however, causes relative cervical lordosis.^{11,12} The normal variation in the ratio of head to body among children results in a range of cervical spine positioning of up to 27° flexion or extension from neutral during immobilization for trauma transport.¹³

There are numerous studies documenting the potential harmful effects of full spinal immobilization. Airway management and ventilation of trauma victims may be encumbered by full spinal immobilization. Cervical spine immobilization has been shown to make direct laryngoscopy three times more difficult compared to manual immobilization during intubation.¹⁴ A study of healthy children who were fully immobilized demonstrated a mean reduction in FVC to 80% of their unrestrained supine FVC.¹⁵ A similar significant decrease in mean FVC has been documented among adults.¹⁶ Full spinal immobilization has been reported to cause substantial pain, which may last well beyond the immediate period of immobilization.^{17,18,19,20} Furthermore, pain caused by spinal immobilization may be confused with pain caused by injury leading to unnecessary diagnostic evaluations. In spine-injured patients, prolonged immobilization is associated with an increased risk of developing pressure sores during the immediate post-injury period.^{21,22} Finally, among head-injured patients, cervical immobilization was associated with a mean rise in ICP of 4.5 mmHg.²³

Once the patient is immobilized, the process of cervical spine “clearance” often involves the use of radiographic procedures. When these procedures are considered in conjunction with

the actual process of spinal immobilization, the cost of immobilization has been estimated at \$440 per patient.²⁴ The expense to the healthcare system is noteworthy when you consider that more than 800,000 patients are immobilized annually in the United States.²⁵ Because of the immaturity of the pediatric spine, plain radiographs are often insufficient for radiographic clearance in children. As a result, computed tomography (CT) and magnetic resonance imaging are utilized for clearance.^{26,27,28} CT, the more common adjunct to conventional radiography of the cervical spine, is associated with considerable exposure to radiation.²⁹ Children are more susceptible to radiation-induced cancers. It is estimated that, depending on age, a pediatric CT increases the population risk of fatal cancer by 4-6 cases per 10,000 pediatric CT examinations.^{30,31,32} Furthermore, for each radiation-induced lethal malignancy, as many as five non-lethal malignancies will be induced.³³

Due to the questionable efficacy and reported adverse effects of spinal immobilization, the risk of irradiation during cervical spine clearance, and the costs associated with spinal immobilization and clearance, there have been some efforts to limit spinal immobilization of trauma patients. Among adults, there is a movement away from the use of criteria for cervical spine immobilization based on mechanism of injury in favor of high-risk clinical screening criteria. The National Emergency X-ray Utilization Study (NEXUS) collaboration developed five clinical screening criteria (posterior midline cervical tenderness, altered alertness, distracting injury, intoxication, and focal neurological findings), which have nearly 100% sensitivity for CSI and good inter-rater agreement among emergency physicians.^{24,25,34,35,36,37} Alternatively, the Canadian C-spine Rule has been reported to have nearly 100% sensitivity for CSI in alert and stable adult trauma patients. The Canadian C-spine Rule screening criteria were based on clinical, epidemiologic, and mechanism of injury variables (ambulatory, ability to sit upright, duration to onset of neck pain, midline cervical tenderness, ability to rotate neck, paraesthesias, and age greater than 65 years, and dangerous mechanism versus simple rear-end collision).^{38,39} Neither of these studies, however, focused on children (fewer than 10% of the NEXUS patients were children, and the Canadian study was of adults only).

While high-risk clinical screening criteria provide promising results in the adults, these findings have not been applied to children due to differing injury patterns, anatomic variance, and age-related differences in the ability to localize pain. High-risk clinical screening criteria for CSI have yet to be adequately identified and evaluated in children. Early attempts at defining pediatric clinical screening criteria have tended to agree with the findings in adult patients, but are not generalizable due to small sample sizes that are not geographically, demographically, or clinically representative.^{40,41,42,43} Furthermore, pre-verbal children who rarely experience CSI are particularly under studied, and are potentially most at risk from inappropriate immobilization.

Beyond the paucity of evidence supporting the use of high-risk clinical screening criteria for CSI in children, the data regarding pediatric CSI prediction in the out-of-hospital setting are particularly lacking. Early studies which include children suggest that when screening criteria are applied in the out-of-hospital setting by paramedics and other Emergency Medical Service (EMS) out-of-hospital workers, the criteria result in a 33% reduction in overall spinal immobilization without missing clinically significant CSI.^{44,45} Despite these promising results, these data are limited, and there are indications that out-of-hospital care providers differ in their ascertainment of clinical screening criteria. Prospective studies evaluating the agreement between EMS workers and emergency physicians for CSI risk are inconclusive with kappa statistics ranging from poor to excellent.^{46,47,48} These findings highlight the limitations associated with developing clinical decision rules in the in-hospital setting that will eventually be

applied to the out-of-hospital environment. Identification of factors which can be reliably observed in the pre-hospital setting will help ensure that clinical decision rules can be applied appropriately in the out-of-hospital setting.^{49,50}

Because there has been insufficient research in CSI and the use of out-of-hospital spinal immobilization in children, and a general lack of involvement of EMS providers in clinical research, there is a need to provide the foundation for a large, definitive clinical trial investigating out-of-hospital spinal immobilization in children after trauma.^{43,44}

The Pediatric Emergency Care Applied Research Network (PECARN) provides the ideal setting to engage in the collaborative investigation of pediatric CSI prediction models.⁵¹ More than 800,000 acutely ill and injured children are cared for annually in the 25 emergency departments (EDs) of this federally-funded research network. Participating EDs are geographically diverse and have the potential for accruing more than 100 children with CSI per year. Research conducted within PECARN has the power and efficiency to develop and test protocols for out-of-hospital pediatric spinal immobilization.

We propose a systematic approach to establishing an evidence-based out-of-hospital spinal immobilization protocol for the transport of pediatric trauma patients. This project entails assembling the largest and most representative cohort of children with CSI. We will compare these children to non-CSI blunt injured children to identify a set of high risk variables that are associated with CSI in children. Children who do not meet a well-validated set of high risk screening criteria are likely to have negligible risk of CSI. These criteria could be used to select children with negligible risk of CSI for future prospective studies designed to compare alternative strategies for safe transport.

Goals and Objectives

The purpose of this study is to identify a set of variables that separate injured children with negligible risk for CSI from those at non-negligible risk for CSI. To achieve our purpose, we have established two specific goals:

Goal 1: To describe CSI among a diverse pediatric population.

Objective 1A: To describe the demographic characteristics, mechanisms of injury, clinical presentations, out-of-hospital management, hospital care and functional outcomes at discharge of pediatric blunt trauma victims with CSI.

Objective 1B: To report a point estimate of the sensitivity of the NEXUS criteria for CSI among a large cohort of pediatric blunt trauma victims with CSI.

Objective 1C: To describe and compare the demographic characteristics, mechanisms of injury, clinical presentations, out-of-hospital management, hospital care, functional outcomes at discharge, and sensitivity of the NEXUS criteria among relevant sub-populations (age, neurological outcome, injury, and out-of-hospital immobilization) of pediatric blunt trauma victims with CSI.

Goal 2: To identify factors associated with increased risk for CSI among a diverse pediatric blunt trauma population.

Objective 2A: To identify clinical and mechanism of injury variables that are associated with increased risk for CSI among pediatric blunt trauma victims.

Objective 2B: To determine if there are age-related or EMS-transport related differences in the clinical and mechanism of injury variables that are associated with increased risk for CSI.

Objective 2C: To identify a set of potential high-risk screening criteria among pediatric blunt trauma victims that will identify all children with CSI, and would decrease

the use of spinal immobilization and radiographic clearance in children at negligible risk for CSI.

Methods:

In order to meet the goals of this study, we will conduct a case-control analysis of CSI among blunt trauma injured children using data collected at a minimum of 20 PECARN sites.

Identification of cases: The medical records for all pediatric patients presenting before their 16th birthday to PECARN affiliated medical centers (study sites) for care of CSI between January 1, 2000 and December 31, 2004 will be eligible for review as cases. The study population will consist of all children within the reference population who have sustained a blunt-trauma related CSI. Each site will identify potential cases through direct query of their patient billing database looking for ICD-9 CSI diagnostic codes (805.0-805.19, 805.8-805.9, 806.0-806.19, 806.8-806.9, 839.0-839.18, 839.40, 839.49, 839.50, 839.59, 839.8, 839.9, 952.00-952.09, 952.8, 952.9, 953.0, 954.0, 953.8, 953.9, 954.8, & 954.9 or 805, 806, 839, 952, 953, 954 without an extension). These codes include injuries to the cervical spinal cord, cervical spinal vertebrae, and ligaments. We will exclude subjects during data abstraction if the injury was: 1) caused by penetrating trauma, 2) the injury occurred during hospitalization, 3) the patient was admitted with a presumed diagnosis of cervical spine injury, which was subsequently ruled-out on further evaluation, or 4) the patient was transferred away from the study site for definitive diagnosis and care elsewhere or the patient was transferred to the study site after definitive diagnosis and care.

Identification of controls: Controls will be drawn from the population of patients presenting to PECARN sites before their 16th birthday for evaluation of blunt trauma during the same time period as the cases who were evaluated with radiography of the cervical spine, and who do not have CSI. Each study site will identify potential controls through a query of their patient billing database searching for patients who have undergone radiographic evaluation for CSI (CPT or ICD-9 procedure codes) and found to be free of spinal cord injury (do not carry the ICD-9 codes for CSI: 805.0-805.19, 805.8-805.9, 806.0-806.19, 806.8-806.9, 839.0-839.18, 839.40, 839.49, 839.50, 839.59, 839.8, 839.9, 952.00-952.09, 952.8, 952.9, 953.0, 954.0, 953.8, 953.9, 954.8, & 954.9 or 805, 806, 839, 952, 953, 954 without an extension). We will exclude patients during data abstraction if: 1) the injuries were caused by penetrating trauma, 2) the injuries occurred during hospitalization, 3) the patient was diagnosed with a CSI that was not ICD-9 encoded for billing, or 4) the patient was transferred away from the study site for definitive diagnosis and care elsewhere or the patient was transferred to the study site after definitive diagnosis and care.

Lists of potential cases and controls, based on the above criteria, will be generated by appropriate IT staff at all participating study sites, in consultation with CDMCC IT staff as needed. A list of potential cases and controls will be submitted to the CDMCC by each study site. Medical record numbers will be converted to "Patient Study IDs" at all centers prior to data submission to the CDMCC. CDMCC will select the controls and send back a list of charts that need to be abstracted. The study site will maintain a master key that links the patient study ID to their institutional medical record number.

Comparison groups: We will create three control groups for comparison. For each study site, the CDMCC, we will use computerized randomization and matching algorithms to identify 2 controls for each child with CSI for each control group. The three control groups will be as follows:

1. A random selection of (unmatched) controls

2. Controls matched to CSI children based on age and mechanism of injury
3. Controls that were brought to the study site by EMS age matched to children with CSI that were brought to the study site by EMS (age matched for subgroup of patients transported by EMS).

Justification for comparison groups: Age has been shown to be associated with risk for CSI, although it has not been found to be a significant predictor of CSI among adults (RR of children <18y = .39).^{43,52} Among children, age is likely to significantly influence the presentation of CSI and false inferences could be made if the age distribution of the control group did not mirror the age distribution among the children with CSI. For example, without matching, there would be a risk of comparing a group of predominately teenagers with CSI to a group of predominately toddlers without CSI; in this situation, attempted statistical adjustment for age may be imprecise. Our first comparison group will allow us to explore age as a risk factor for CSI. For the subsequent comparison groups, we will age match to the control that has a DOB closest to the CSI case and has a match for mechanism of injury or EMS transport.

Particular mechanisms of injury are known to put patients at higher risk of injury such as high speed automobile collisions or ejection from an automobile. Mechanism of injury, however, has not been shown to be efficient in the prediction of specific injuries, particularly CSI. The unmatched group will allow us to explore the relationship of mechanism of injury and CSI. A group matched on mechanism of injury will give us more statistical power to detect demographic or clinical variables that are more efficient at predicting CSI. Matching for mechanism of injury will occur using ICD-9 E-code groupings.

Cases and controls brought to the study site by EMS represent a population of children with higher acuity of care and patients that would be eligible for out-of-hospital spinal immobilization. Our third comparison group allows us to identify variables that are observable in the out-of-hospital setting and are more specific for CSI among patients transported by EMS.

Procedures for Control Selection: For each identified potential case, the CDMCC will generate a list of potential controls, ranked according to closeness of match, starting with the “best” possible match. While two controls of each type will be ultimately selected, additional potential controls will be available in the event that a control must be excluded because of information obtained during the abstraction process. The pool of potential controls is expected to be sufficiently large that these lists can be generated without replacement (i.e., no potential control will appear on a list for more than one case). The RA will examine potential controls in sequential order; therefore, the two ultimately eligible “best matches” will become the final study controls. Lists of potential controls will be generated as follows:

1. Random unmatched controls: For each identified potential case, a list of 5 potential controls will be selected at random from all identified controls at the same center.
2. Controls matched on age and mechanism of injury: For each potential case, the CDMCC will rank all potential controls with the same mechanism of injury category according to the difference in age in days between the control and the case; 10 potential controls will be generated for each case.
3. Controls brought to the study site by EMS: For each case brought by EMS, the CDMCC will rank all potential controls brought in by EMS according to the difference in age in days between the control and the case; 5 potential controls will be generated for each case within this study subgroup. There will be centers for which EMS status will not be known until the time of case record abstraction. For such centers, the CDMCC will provide for every potential case a list of 10 potential controls, ranked according to the difference in age in days between the

control and the case. For the cases identified during the abstraction process as brought in by EMS, the RA will use this list to find the best age-matched controls that were also brought in by EMS.

Data abstraction: After site specific IRB approval, trained on-site personnel will abstract the data from existing medical records by using a HIPAA compliant web-based data collection and storage system. Data sources will include emergency department medical records, hospital admissions record, ICD-9 and CPT billing codes for the injury encounter, and EMS “run sheets” when available. The data to be collected include demographic characteristics, pre-existing conditions, injury mechanism, clinical presentation at the study site, CSI characteristics, concomitant injuries, clinical interventions, complications during hospitalization, and clinical outcomes at hospital discharge. For the subset of patients who were transported to the study site by out-of-hospital EMS providers and have run sheets available for data abstraction, clinical findings at presentation in the field will be recorded separate from the findings identified in the emergency department. For patients who have been transferred to the participating site from an outside hospital for definitive care and have outside hospital medical records available for review, we will record clinical findings at presentation and clinical interventions. Site personnel will be blinded to the cumulative study results.

Data Quality-: The CDMCC will be responsible for quality assurance during the study. . A CDMCC study coordinator will produce and disseminate weekly progress reports for each study site which details the number of completed charts. Data queries will be developed to identify and resolve potential data inconsistencies. A CDMCC site monitor will visit each study site during the study period and review chart identification, abstraction, and record maintenance to assure compliance with the study methodology and adherence to Good Clinical Practice guidelines. The CDMCC will coordinate the re-abstraction of charts by each study site to allow calculation of a kappa statistic, a measure of inter-rater reliability for the data abstraction.

Case Evaluation: We will conduct a separate analysis for the entire case cohort as well as for clinically relevant sub-samples within the cohort. These sub-samples will be based on: age (birth to day prior to 8th birthday, 8th birthday to day prior to 16th birthday), neurological outcome (no sequelae, moderate sequelae, and severe sequelae), injury (clinically significant and clinically non-significant determined by criteria established during the NEXUS and Canadian C-spine collaborations²³), and out-of-hospital immobilization (immobilized versus non-immobilized). We will report descriptive statistics for all individual variables as frequencies and percentages for categorical measures and means with standard deviations for continuous measures. The proportion of patients with CSI who have one or more of the NEXUS high-risk screening criteria will be reported as a point estimate of the sensitivity of the NEXUS criteria in this cohort. We will compare normally distributed continuous outcome measures among age, immobilization, injury severity, and neurological outcome strata using a Student’s t-test. We will use appropriate non-parametric techniques for non-normally distributed data. We will compare categorical measures using chi-square analyses, including exact methods when appropriate.

Control Evaluation: For the controls, by group, we will report descriptive statistics for all variables as appropriate: frequencies and percentages for categorical measures and means with standard deviations (or medians and interquartile range) for continuous measures.

Case-control Comparisons: Prior to multivariate analysis for all comparison groups, we will perform univariate logistic regression analysis, calculating odds ratios and 95% confidence intervals for each independent variable in separate models. Variables with odds ratios that have

p-values ≤ 0.25 in bivariate analyses will be considered as candidate predictors for the multivariate models. We will build the final multivariate model in the following manner:

1. Comparison of cases to unmatched controls: For multivariate analysis that includes cases and unmatched controls, we will use standard multiple logistic regression analysis. Starting with the pool of predictors that showed at least a weak trend of univariate association with outcome, we will use stepwise selection approaches to identify demographic characteristics, mechanisms of injury, and clinical presentation variables that significantly independently contribute to the identification of children with CSI. We will conduct this analysis for the entire comparison group and with age-stratification (age < 8years and 8-16 years).

2. Comparison of cases with age and mechanism matched controls: We will employ similar stepwise selection approaches, using conditional logistic regression analysis.

3. Comparison of cases brought to the study site by EMS with age-matched controls that were brought to the hospital by EMS: We will employ the stepwise selection approach, once again using conditional logistic regression.

To determine the fit of the regression models, we will calculate standard goodness-of-fit statistics and receiver-operator characteristics (ROC) of various models. The pseudo- R^2 will be used as an indicator of the proportion of the variance explained by the models. Logistic regression model diagnostics will also be performed to assess the presence and effect of potential outliers; these will be identified by use of measures such as deviance residuals and leverage statistics. The Hosmer and Lemeshow test will also provide some evidence of the goodness of fit of the final models to the dataset. These approaches are generalizable to the conditional logistic model.^{53,54}

An ROC curve will be constructed for the final models. This will identify variables that had the greatest ability to distinguish patients with CSI from those without such injury. Once a model is fit, beyond examining the area under the ROC curve, which gives a general feel for how well the model performs, we will examine its sensitivity and specificity. As this is not a cohort study, we will not be able to explore the positive and negative predictive values of the resulting model. Because CSI is such a rare outcome, however, and the odds ratio approximates the relative risk of diseases that have a very low incidence, we will be able to make estimates of the relative risk of CSI in the presence versus absence of specific variables.

Missing Data: Although we will make every effort to obtain data for all independent variables, we expect that some subjects will have missing data for at least some variables that are significant univariate or multivariate predictors of outcome. The best solution to this problem in our specific setting will be determined by the number of potential predictors and the proportion of missing data for each.^{55,56} A variable with very high proportion of missing data (for example, 50%) is likely inadvisable for consideration as a potential predictor (in fact, if it is not available in the “real world” clinical setting a large proportion of the time, it would not qualify as a useful predictor in any case). If an important variable is not available for a relatively small proportion of subjects, imputation may be a useful approach to allow some assessment of the potential contribution of a case with missing data to the analysis. If neither the presence nor the absence of a very rare risk factor is documented in the medical record, it may be reasonable to assume that this factor is absent in some settings. In the case of an important measure (continuous or categorical) whose value is unknown for a subject, but which tends to be strongly correlated with other factors whose values are known for that child, multiple imputation may be an option.

Generally, we are most confident with predictions that are made from a complete-case analysis, and would use imputation approaches to gauge the robustness of this analysis to

information available from other cases. Comparison of key characteristics including outcomes between subjects in the final multivariable model, and those excluded from this model due to missing data will also provide insight regarding generalizability of the findings.

Case-Control Sample Size: The medical records of 550 children with CSI following blunt trauma from January 1, 2000 through December 31, 2004 will be reviewed at 20 PECARN sites. This sample size is based on the need to meet the first 2 sets of goals and objectives:

Goal 1, Objective 1A: To describe the pediatric CSI population with particular focus on the clinical presentation and emergency management of these patients. To date, this would be the largest and most geographically and demographically diverse retrospective case-series of CSI among children. Previous studies focusing on the clinical presentation of children with CSI had samples that were an order of magnitude smaller than proposed by this study (Racheksky et al N = 25, Jaffe et al N = 59, Viccellio et al for NEXUS N = 30).^{35,36,37}

Goal 1, Objective 1B: To provide a point estimate of the sensitivity of the NEXUS criteria in children with CSI. Within this cohort, 405 CSI subjects are needed to provide an estimate of the sensitivity of the NEXUS criteria that we are 95% confident falls within 0.05% of the true estimate. Based on our pilot abstraction we anticipate that 467 of the 550 children with CSI will have the complete set of NEXUS clinical findings documented enabling us to meet these tight confidence intervals for the point estimate of sensitivity.

Goal 1, Objective 1C: To describe and compare the clinical presentation of children with CSI among relevant subpopulations within this cohort. Perhaps the most important of these subpopulations is children younger than eight years of age, an age group which is under-represented in the medical literature. This younger cohort of patients has age-related anatomic and cognitive differences that may influence their injury patterns and presentation. A sample of 550 children with CSI is needed to demonstrate a two-fold difference in the presence of focal neurological findings between the under 8 year-olds and 8 to under 16 year-olds. We based this sample size calculation on a power = 0.80 and $\alpha=0.05$ in order to detect a odds ratio for focal neurological findings of 2.0 or larger between the subpopulations within the case-series.^{57,58} The proportion of other findings among subjects is expected to be at least 20%, which will result in the ability to detect smaller odds ratios with the same number of patients. Further, at this sample size, we will have 80% power at $\alpha=0.05$ to detect an odds ratio for focal neurological findings of 3.0 or larger between CSI children that are younger than 2 years and CSI children that are 2 to 16 years.

Goal 2, Objectives 2A, 2B, 2C: To identify factors that are associated with increased risk for CSI among a diverse pediatric blunt trauma population. Using a 1:2 matched case-control design to meet the specific objectives of the case-control analyses, a minimum of 450 children with CSI and 2,700 non-CSI children are needed. This estimate is based on sample size calculations with power 0.99 and $\alpha=0.05$ in order to detect odds ratios for focal neurological findings of 2.0 or larger.^{58,59} We relied upon the NEXUS data to estimate the prevalence of focal neurological findings among controls (10%) and subjects (20%) which was used to calculate sample size.^{58,59} The proportion of other findings among controls is expected to be at least 20%, which will result in smaller odds ratios able to be detected with the same number of patients. At this sample size, it is feasible that we can identify a set of potential high-risk criteria that have a sensitivity of 99.7% (CI 98.3-99.98%) for CSI.

Case-Control Significance: A case-control study is the logical first step in a broader effort to establish a basis for limiting the unnecessary and potentially harmful practice of full spinal immobilization among pediatric blunt trauma victims who are at negligible risk for CSI.

This study will be the largest, by an order of magnitude, multi-centered retrospective case-control study describing the mechanism of injury, clinical presentation, pre-hospital and hospital interventions, and outcomes of cervical spine-injured children. If the NEXUS criteria are nearly 100% sensitive for CSI in these children with CSI, we have the initial evidence for supporting the investigation of these criteria as high-risk screening criteria for CSI among pediatric trauma victims. If the NEXUS criteria perform poorly among the cohort, we have a large enough sample to identify characteristics that occur at a high frequency among children with CSI and can investigate them as risk factors for CSI among blunt-trauma injured children using the case-control methodology.

This study will establish the basis for limiting the unnecessary and potential harmful practice of full spinal immobilization among pediatric blunt trauma victims at negligible risk. It will represent the absolute largest and first multi-centered retrospective case-control study identifying predictive variables for CSI among children. Observations regarding these characteristics will be used to build a model of high-risk screening for CSI among children that will be validated in subsequent randomized clinical trials of pediatric spinal immobilization in the out-of-hospital and emergency department settings.

Commitment to Human Subjects' Protection All key personnel involved in the design or conduct of the research involving the human subjects will receive the required education on the protection of human research participants prior to funding of this project. IRB approval will be obtained from all governing bodies for participating PECARN sites prior to conducting study initiation. Research records will be de-identified and maintained in secure encrypted HIPAA compliant databases.

Key Organizations and Advisory Committee This study utilizes PECARN, a collaborative pediatric emergency medicine research group formed from 25 medical centers across the United States. The infrastructure of this network is funded through HRSA. We have formed an advisory committee from within PECARN that includes a case-control methodologist (Nate Kuppermann), a biostatistician (Richard Holubkov), a pediatric trauma care specialist (Art Cooper), and representatives from each of the regional groupings within PECARN (Project PIs, Kathleen Brown, Prashant Mahajan, and Lynn Babcock-Cimpello). The Central Data Management Coordinating Center, a HRSA funded center affiliated with PECARN, will provide data management and site monitoring.

Study Dissemination Plan We will share the findings of this study with both the medical and lay communities through research symposiums, peer-reviewed journals, and appropriate media channels.

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