# Development and Testing of a Pediatric Cervical Spine Injury Risk Assessment Tool (C-Spine) PECARN Protocol Number 042

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PROTOCOL TITLE:

Development and Testing of a Pediatric Cervical Spine Injury Risk Assessment Tool

Short Title: C-Spine
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*I confirm that I have read this protocol, I understand it, and I will conduct the study according to the protocol. I will also work consistently with the ethical principles that have their origin in the Declaration of Helsinki and will adhere to the Ethical and Regulatory Considerations as stated. I confirm that if I or any of my staff are members of the Institutional Review Board, we will abstain from voting on this protocol, its future renewals, and its future amendments.*

Principal Investigator Name: _____

Principal Investigator Signature: _____

Date: _____

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**Abstract**

Cervical spine injuries (CSI) are serious, but rare events in children. In contrast, use of spinal precautions for trauma transport and radiographic evaluation for CSI in the emergency department (ED) are common and associated with adverse effects. As a result, millions of children who have no CSI are exposed to harm with no demonstrable benefit. The nation's EMS systems need a Pediatric CSI Risk Assessment Tool that can be used to reduce the number of children who are transported in spinal precautions and irradiated unnecessarily. Leonard et al. and the Pediatric Emergency Care Applied Research Network (PECARN) retrospectively identified 8 risk factors that predict CSI in children. Leonard et al. also established the infrastructure to prospectively collect paired observations from EMS and ED providers and determined the test accuracies of the PECARN CSI risk factors. This study proposes to develop and test a Pediatric CSI Risk Assessment Tool that can be used by EMS and ED providers to determine which children warrant spinal precautions and cervical spine imaging after blunt trauma.

Leonard et al. will conduct this work at approximately 18 PECARN trauma centers and collect prospective observational data from EMS and ED providers regarding CSI risk factors for children who undergo emergency evaluation after blunt trauma and follow enrolled subjects for 28 days to determine CSI status. The study will occur in two phases: development (13,333 children; 240 children with CSI) and validation (8,889 children; 160 children with CSI). The study will also capitalize on the research infrastructure to conduct an Applied Cognitive Task Analysis (ACTA) and tool prototype testing that will inform the iterative tool design to ensure that the tool is useable by EMS and ED providers. With data from the development cohort, a useable clinical decision support tool will be constructed that achieves $>$ 95% sensitivity, as well as adequate specificity ($>$ 40%) in the prediction of CSI. Subsequently, Leonard et al. will determine the performance characteristics of the tool in the independent validation cohort and in a cohort that has EMS provider observations. The ultimate output from this project will be a set of specifications for the Pediatric CSI Risk Assessment Tool that will include a validated clinical decision rule, validated tool designs and functions, and recommendations for implementation. An accurate, validated, and ultimately field-tested Pediatric CSI Risk Assessment Tool will safely limit unnecessary spinal precautions and radiographic testing for millions of children while helping identify those children who are truly at risk for CSI.

# 1 Study Summary

Cervical spine injuries (CSI) are serious, but rare events in children.[1, 2] Spinal precautions (rigid cervical collar and immobilization on a longboard) in the prehospital setting

may be beneficial for children with CSI, but are poorly studied.[3–6] In contrast, spinal precautions for pediatric trauma patients without CSI are common and may be associated with harm.[5, 7–32] Spinal precautions result in well-documented adverse physical and physiological sequelae.[5, 7–31] Of substantial concern is that the mere presence of prehospital spinal precautions may lead to a cascade of events (see conceptual model, Figure 1) that results in the increased use of inappropriate radiographic testing in the emergency department (ED) to evaluate children for CSI and thus an unnecessary, increased exposure to ionizing radiation and lifetime risk of cancer.[29–31, 33–56] Most children who receive spinal precautions and/or are imaged for potential CSI, and particularly those imaged with computed tomography (CT), are exposed to potential harm with no demonstrable benefit. Therefore, there is an urgent need to develop a Pediatric CSI Risk Assessment Tool that can be used in the prehospital and ED settings to reduce the number of children who receive prehospital spinal precautions inappropriately and are imaged unnecessarily while identifying all children who are truly at risk for CSI.[6, 57–68]

## 1.1 Specific Aims

The goal of the current project is to develop and test a Pediatric CSI Risk Assessment Tool that can be used by EMS and ED providers to determine which children warrant spinal precautions and cervical spine imaging after blunt trauma. We will use the R21-established research infrastructure to conduct a larger multi-center, prospective observational cohort study and an applied cognitive task analysis to inform a process of iterative tool design that has the following Specific Aims:

**Specific Aim 1.** Develop the Pediatric CSI Risk Assessment Tool in children with blunt trauma using prospective observational data obtained from ED providers.

**Specific Aim 2.** Validate the Pediatric CSI Risk Assessment Tool in a separate population of children with blunt trauma using prospective observational data obtained from ED providers.

**Specific Aim 3.** Validate the Pediatric CSI Risk Assessment Tool in a population of children with blunt trauma using prospective observational data obtained from EMS providers.

## 1.2 Subject Eligibility, Accrual and Study Duration

Eligible participants will be identified by study staff. Patients will be enrolled in the study if they meet the following inclusion criteria:

1. Age 0-17 years; AND
2. Known or suspected exposure to blunt trauma regardless of whether or not injuries were sustained; AND
3. One of the following:
   (a) Undergoing trauma team evaluation; OR
   (b) Transported from the scene to site facility by EMS; OR
   (c) Undergoing cervical spine imaging at site facility; OR
   (d) Transferred to site facility with cervical spine imaging.

Patients will be excluded from enrollment if they meet the following exclusion criteria:

1. Exposed to solely penetrating trauma mechanism (example: gunshot or stab wound)*

   *Note that children that have sustained penetrating injuries as a result of or in addition to a blunt trauma mechanism are not excluded from eligibility.

# 2 Rationale and Background

## 2.1 Introduction and Study Rationale

***Spinal precautions are the standard of care for trauma patients but have questionable efficacy.*** Historically, spinal precautions were 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 spinal motion during transport will prevent or limit neurological injury.[3] This practice, however, is poorly studied and may be harmful. Even for the rare child who has sustained a CSI, the efficacy of spinal precautions in limiting neurological injury during emergency medical services (EMS) transport is unknown.[4] A Cochrane review concluded that "the effect of prehospital spinal immobilization on mortality, neurological injury, spinal stability and adverse effects in trauma patients remains uncertainthe possibility that immobilization may increase mortality and morbidity cannot be excluded."[4] In fact, there is evidence that challenges the efficacy of spinal precautions in providing neutral positioning and in limiting neurological injury for those patients with CSI.[4, 5, 7–14] Furthermore, for those at greatest risk of CSI, spinal precautions are associated with adverse side effects including encumbered airway management and ventilation, elevated intracranial pressure and decubitus ulcers.[15–25] Thus, while spinal precautions for trauma transport are considered the standard of care, there is no evidence supporting their use and some evidence illustrating adverse effects.

***Spinal precautions cause harm for those children at low risk for CSI by increasing self-reported pain and prompting reliance on radiographic studies to evaluate for CSI.*** EMS providers use spinal precautions somewhat indiscriminately which is concerning as spinal precautions are associated with adverse effects.[32] The most common adverse effect of spinal precautions is musculoskeletal pain. Immobilization on a rigid longboard and placement of a rigid cervical collar causes substantial pain, which may last well beyond the immediate period of immobilization.[26–31] The pain caused by spinal precautions may be confused with pain caused by injury leading to unnecessary diagnostic evaluations.[30, 31] Additionally, the presence of spinal precautions at the time of evaluation may heighten physician concern for CSI and/or interrupt a useful neck examination.[30] Further magnifying the situation is that 70% of children are cared for by adult-oriented trauma surgeons and general emergency medicine providers when the trauma system is activated and there is an impulse to use neck CT for CSI screening, a practice that is supported in the adult trauma patient.[33] Thus, given the lack of established guidelines for clinical clearance of CSI in children, ED and other providers may overly rely on radiographic imaging for diagnostic evaluation.[30, 33–35] This cascade of events, prehospital spinal precautions followed by use of radiographic imaging for clearance of CSI (Figure 1 on the following page), results in potential harm for most children who present for care following blunt trauma.

***Reliance on CT scanning to evaluate the cervical spine in children who are at low risk for CSI results in substantial exposure to ionizing radiation and increased risk of cancer.*** Due to a general apprehension that the immaturity of the pediatric spine will limit the interpretability of plain radiographs and that some important injuries may be missed, CT scanning, which is associated with substantial exposure to radiation, is frequently used to evaluate children for potential CSI.[33–38] Children are more susceptible to radiation-induced cancers due to an intrinsic sensitivity to ionizing radiation and a longer life expectancy during which the cancer may manifest.[39–42] It is estimated that, depending on age, pediatric CT increases the population risk of fatal cancer by 4-6 cases per 10,000 pediatric CT scans.[43–49] Furthermore, for each radiation-induced lethal malignancy, as many as 5-10 non-lethal malignancies will be induced.[43–49, 56] CT scans of the neck are of particular concern in children because of a well-documented, age-related radiation sensitivity of the thyroid due to its size relative to surrounding structures, proportion of dividing cells, and concentration by iodine.[50–55] A single CT scan of the cervical spine in childhood is associated with significant thyroid irradiation, increasing a child's lifetime risk of thyroid cancer by 78%.[56]

***Adult CSI screening criteria have been derived and validated for use in limiting radiographic imaging during ED trauma evaluation.*** Due to both the risk of irradiation during cervical spine evaluation and its cost, there have been

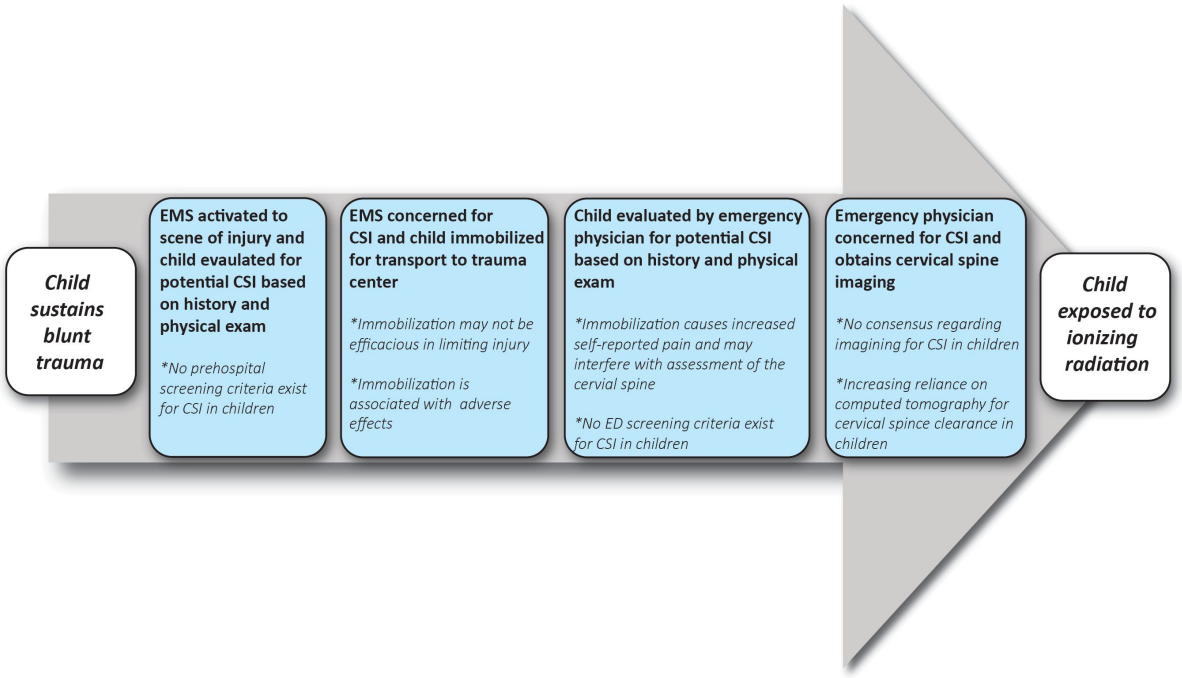


Figure 1: Evaluation of children for CSI following blunt trauma

considerable efforts to limit radiographic clearance of adult trauma patients. The National Emergency X-ray Utilization Study (NEXUS) collaboration developed a predication rule with five clinical screening criteria (posterior midline cervical tenderness, altered alertness, distracting injury, intoxication, and focal neurological findings), which has 100% sensitivity for CSI and exhibited good inter-rater agreement among emergency physicians.[69–72] In addition, the Canadian C-spine Rule (ambulatory, ability to sit upright, time to onset of neck pain, midline cervical tenderness, ability to rotate neck, paresthesia, age older versus younger than 65 years, and dangerous mechanism versus simple rear-end collision) has been reported to have nearly 100% sensitivity for CSI in alert and stable adult trauma patients.[73–76] Neither of these studies, however, focused on children. The NEXUS study had only 30 children with CSI and the Canadian study excluded pediatric patients.

***EMS prehospital providers can appropriately apply adult CSI screening criteria, but their reliability in assessing CSI screening criteria has not been demonstrated.*** Early studies suggest that when adult screening criteria are applied in the prehospital setting by EMS providers, the criteria result in a significant reduction (up to 50%) in overall spinal immobilization without missing clinically important CSI.[77–80] Despite these promising results, there are indications that EMS prehospital providers differ in their ascertainment of clinical screening criteria. Prospective studies evaluating the agreement between EMS providers and emergency physicians for adult CSI risk are inconclusive with kappa statistics ranging from poor to excellent.[81, 82] These findings highlight the limitations associated with developing clinical decision rules exclusively in the ED setting that are intended to also be applied in the prehospital environment. Involvement of EMS prehospital providers early in the development and/or refinement of clinical decision rules will help ensure that the rules can be applied appropriately in the prehospital setting.[83–86]

***Clinical screening criteria for CSI in children are lacking.*** While clinical screening criteria provide promising results in adult trauma patients, these findings should not be applied to children due to differing injury patterns, anatomic variance, and age-related differences in the ability to localize pain. Clinical risk stratification criteria for CSI have yet to be adequately identified and evaluated in a prospective fashion 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.[2, 87–89] Particularly under represented in previous studies are pre-verbal children who rarely experience CSI, but are potentially at greatest risk from inappropriate immobilization and imaging.[2, 87–89] As a result, more than eight million injured children in the U.S. annually are evaluated for potential CSI and may be subject to spinal precautions and/or radiographic imaging yet fewer than one percent will actually have CSI.[2, 58]

In sum, there has been insufficient research in CSI evaluation and management in injured children in both the prehospital and ED settings. In particular, there are no established clinical screening criteria for CSI in children, and as a result, many children are exposed to spinal precautions and radiographic evaluation unnecessarily. Because of this, and the alarming increase in CT use in children, ***there is an urgent need to develop and implement a Pediatric CSI Risk Assessment Tool that can be used by EMS and ED providers to determine which children warrant spinal precautions and cervical spine imaging after blunt trauma.***

## 2.2 Preliminary Studies

With federal funding, Pediatric Emergency Care Applied Research Network (PECARN) investigators, led by this study's Principal Investigator (PI), conducted a large retrospective case-control study of children with CSI which allowed us to identify a set of risk factors that are significantly associated with CSI.[90, 91] These factors; altered mental status, focal neurological deficits, self-report of neck pain, torticollis, substantial injury to the torso, predisposing condition, high-risk motor vehicle crash, and diving mechanism; had greater than 98% sensitivity for identifying all children with CSI in the cohort. If these mechanistic and clinical factors were used as clinical screening criteria for CSI, radiographic imaging for CSI in the cohort would have been reduced by more than 25%. These factors, however, need prospective evaluation and refinement prior to implementation as a risk assessment tool that guides management. In order to develop a risk assessment tool for CSI in children, a large prospective cohort of children experiencing blunt trauma is required due to the rarity of CSI.

As a prerequisite for a large, prospective multi-center study to develop and validate a Pediatric CSI Risk Assessment Tool, we conducted a NICHD R21-funded, 4-center (Washington University in St. Louis, Medical College of Wisconsin, Cincinnati Children's Hospital Medical Center and Nationwide Children's Hospital) pilot study aimed at developing the infrastructure (materials, methods and procedures) necessary for collecting prospective data from prehospital EMS providers and ED providers who care for children after blunt trauma.[92] We developed a web-based, branch-logic questionnaire using Research Electronic Data Capture (REDCap) that was administered via a tablet computer to ED providers (attending or fellow pediatric emergency medicine, emergency medicine or hospitalist physicians, or advanced practice nurses or physician assistants) during their ED evaluation of children with blunt trauma, and if applicable, to the EMS providers who had rendered scene response care.[92, 93] The questionnaire assessed factors determined a priori to be associated with CSI in children, including those from our retrospective case-control study.[69, 73, 90, 91, 94, 95] We collected data in the ED under waiver of informed consent;

however we provided parents/guardians a study information sheet with instructions for withdrawal from further phone follow-up.[92, 96–99] For children who had cervical spine imaging, we determined presence of CSI by review of the imaging reports by the Site PI with verification of the CSI through review of the spine surgeon's consultation notes. For those children who did not undergo cervical spine imaging in the ED, we made telephone follow-up calls 21-28 days after the ED visit to confirm that the child was free of CSI. To determine whether or not our cohort was representative of all children meeting inclusion criteria, we reviewed daily ED census reports to identify missed eligible children and gathered a limited data set.

Preliminary results from this pilot study support the feasibility of conducting a larger investigation using these established methods. We enrolled 4091 children over 18 months; 84.9% of eligible subjects during enrollment hours and 70.9% of all eligible subjects.[92] The characteristics of those children that we enrolled were comparable to those that were missed.[92] We captured the EMS provider's observations 60.2% of the time for those that arrived as a scene response. Importantly, there were 74 children within the cohort ultimately diagnosed with CSI (1.1 injuries per site per month; CSI incidence of 1.8%).[92]

Table 1 on the next page demonstrates the prospective performance of our retrospectively-identified risk factors in identifying all children with CSI.[94, 95] For each candidate risk factor, we calculated bivariable relative risks. We explored the PECARN model for CSI as a predictor set and considered children with at least one positive risk factor test positive for CSI risk. The PECARN model risk factors were 90.5% sensitive and 45.6% specific for CSI in the cohort. Retrospective medical record review of the 7 children missed by the PECARN model revealed that all either had a PECARN model risk factor that was not captured in the observational data (n=6; altered mental status and complaint of neck pain) and/or had one of the other observed candidate risk factors (n=5; axial load biomechanics, loss of consciousness, other signs of substantial head injury- skull fracture, upper thoracic tenderness and pain). These findings confirm our previously-identified risk factors for CSI in children.

There are several other candidate risk factors (axial load, loss of consciousness, skull fracture, hypoxia, respiratory distress/failure, or intubation) which provide opportunities to improve the PECARN model.[90, 91, 94, 95] Our pilot work supports the prospective refinement of a decision rule based on these risk factors that will serve as the basis for a risk assessment tool for CSI in children after blunt trauma.

While it is reassuring that the PECARN model risk factors performed well when applied to the subsample of patients that had EMS provider observations (Page 16), inter-observer agreement between EMS and ED provider observations was variable and affected by observer group bias and risk factor prevalence.[100, 101] Prehospital use of a pediatric CSI risk assessment tool may be feasible; however agreement on infrequently

| Risk Factors | EMS PROVIDERS (n = 1372) | | ED PROVIDERS (n = 4091) | |
|---|---|---|---|---|
| | Bivariable RR (CI) | PECARN Model Multivariable OR (CI) | Bivariable RR (CI) | PECARN Model Multivariable OR (CI) |
| **Mechanism of Injury/Biomechanics** | | | | |
| High risk MVC* | 1.9 (0.7-5.5) | 2.0 (0.7-5.8) | 1.6 (0.6-3.8) | 1.6 (0.6-4.0) |
| Diving injury | ∞ | ~ | 13.7 (5.6-33.3) | 17.6 (5.6-55.3) |
| Axial load | 5.0 (2.3-10.9) | ~ | 3.2 (1.7-5.8) | ~ |
| Clothes-lining | ∞ | ~ | 3.3 (1.1-10.1) | ~ |
| **History** | | | | |
| Predisposing conditions | ∞ | ~ | 2.0 (0.3-13.8) | 2.0 (0.3-15.1) |
| Loss of consciousness | 1.8 (0.8-4.3) | ~ | 2.1 (1.3-3.4) | ~ |
| Neck pain | 0.8 (0.4-1.9) | 0.8 (0.4-1.9) | 1.6 (1.0-2.6) | 1.7 (1.0-2.6) |
| Inability to move neck | 1.5 (0.4-6.2) | 1.5 (0.4-6.5) | 3.6 (2.0-6.6) | 3.8 (2.0-7.1) |
| **Physical Examination** | | | | |
| Altered mental status | 4.9 (2.3-10.7) | 5.1 (2.3-11.4) | 5.4 (3.4-8.4) | 5.7 (3.5-9.1) |
| Signs of substantial head injury other than altered mental status | 1.9 (0.5-7.7) | ~ | 0.4 (0.1-1.6) | ~ |
| *Signs of basilar skull fracture* | 8.1 (1.3-52.0) | ~ | 5.5 (2.3-13.1) | ~ |
| Posterior midline tenderness to palpation | 0.9 (0.3-2.4) | ~ | 1.5 (0.9-2.3) | ~ |
| Limited neck range of motion | 2.2 (0.8-6.4) | 2.3 (0.8-6.8) | 1.8 (0.9-3.8) | 1.9 (0.9-3.9) |
| Substantial torso injury | 6.8 (2.9-15.8) | 7.4 (3.0-18.4) | 2.5 (1.2-5.2) | 2.6 (1.2-5.5) |
| Substantial thoracic injury | 14.6 (6.3-33.9) | ~ | 5.7 (2.4-13.6) | ~ |
| *Respiratory distress* | 18.6 (6.6-52.2) | ~ | 13.7 (5.6-33.3) | ~ |
| *Decreased oxygen saturation* | 28.9 (12.4-67.1) | ~ | 15.7 (5.8-42.3) | ~ |
| Substantial abdominal injury | 1.6 (0.2-11.4) | ~ | 1.9 (0.7-5.0) | ~ |
| Thoracic spine tenderness | 0.7 (0.2-2.9) | ~ | 1.1 (0.6-1.9) | ~ |
| Focal neurological deficits | 1.6 (0.4-6.5) | 1.6 (0.4-6.9) | 2.6 (1.1-6.2) | 2.6 (1.0-6.6) |
| **Model Performance** | | | | |
| **Sensitivity** | 96.0% (88.3-103.7) | | 90.5% (83.9-97.2) | |
| **Specificity** | 38.5% (35.9-41.1) | | 45.6% (44.0-47.1) | |
| **Negative Predictive Value** | 99.8% (99.4-100.2) | | 99.6% (99.3-99.9) | |
| **Positive Predictive Value** | 2.8% (1.7-3.9) | | 3.0% (2.3-3.7) | |

*Intrusion, including roof; > 12 inches occupant site, > 18 inches any site; Ejection (partial or complete) from automobile; Death in same passenger compartment; Vehicle telemetry data consistent with a high risk of injury
∞Unable to be calculated due to low prevalence

Table 1: Prospective test accuracies of pediatric CSI risk factors

| Intervention | Reported by ED provider for total cohort | Reported by ED provider for cohort presenting directly to the ED | Reported by ED provider for cohort transferred to ED from other facility | Observed on Medical Record Review | With use of the original PECARN Model[91] | |
|---|---|---|---|---|---|---|
| **Spinal precautions[#]** | 1076/1371 (78.5%) | 1076/1371 (78.5%) | Not Applicable | Not Applicable | 767/1371 (55.9%)* | |
| **Any Imaging** | 2723/4091 (66.6%) | 2067/3138 (65.9%) | 656/953 (68.8%) | 3201/4091 (78.2%) | 2253/4091 (55.1%)[¥] | |
| **Plain x-rays** | 2601/4091 (63.6%) | 2094/3138 (66.7%) | 507/953 (53.2%) | 2883/4091 (70.5%) | ED provider | Observed |
| | | | | | 1737/4091 (42.5%)* | 1885/4091 (46.1%)* |
| **CT scan** | 437/4091 (10.7%) | 177/3138 (5.6%) | 260/953 (27.3%) | 648/4091 (15.8%) | ED provider | Observed |
| | | | | | 306/4091 (7.5%)* | 449/4091 (11.0%)* |

[#]Denominator is those children transported from the scene of injury to the study site ED

*Estimated by applying the model to those that had the intervention in the cohort, with the presence of any model variable indicating need for the intervention, and absence of all variables indicating intervention unneeded

[¥]Estimated by applying model to entire cohort, with the presence of any model variable indicating need for imaging, and absence of all variables indicating imaging unneeded

Table 2: Rates of spinal precautions and imaging

encountered factors and on patients whose histories and examinations change over time is complicated. Our pilot work demonstrates that a pediatric CSI decision rule that will be used in the prehospital setting needs to be validated with EMS assessments and supports the need to continue the inclusion of EMS provider's observations in future studies.

Finally, our pilot study established the baseline use of spinal precautions and cervical spine imaging in children after blunt trauma (Table 2). Clinicians used imaging to screen 75.7% of children for CSI after blunt trauma including 15.8% screened by CT. This confirms our concern for some indiscriminate use of cervical spine imaging but also establishes the feasibility of a decision rule that can serve as the basis for a tool that reduces imaging, particularly CT. Rates of CT use were higher for children evaluated at outlying hospitals prior to presenting in the study site EDs (27.3%) with most undergoing imaging prior to transfer. This is important because 90% of children in the U.S. are evaluated in general EDs after blunt trauma and not pediatric EDs.[101, 102] Based on conservative estimates, use of the PECARN risk factors to determine the need for imaging within our pilot study cohort would have reduced overall imaging rates by more than 25% and would have reduced CT use by up to 50%. A tool based on a refined decision rule and that stratifies children by risk to specific imaging strategies, once implemented,

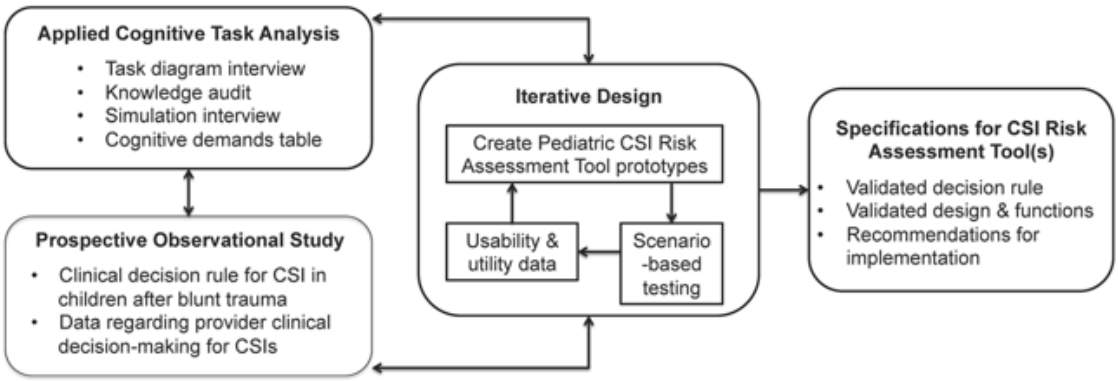


Figure 2: User-centered Approach to Tool Design

would likely result in even further reductions in imaging.

# 3 Overall Study Design

Our project will follow a comprehensive user-centered design approach (Figure 2) that will engage representative clinical end-users in a sequence of activities that provides the following: 1) a decision rule comprised of a parsimonious set of risk factors that predict CSI in children after blunt trauma and that meet the analytic hypotheses tied to our specific aims, 2) defined relevant clinical roles associated with evaluating children for CSI, 3) descriptions of the clinical scenarios in which children are evaluated for CSI, 4) a detailed cognitive task analysis of the clinical workflow involving all clinical roles and scenarios, 5) decision tool prototypes suitable for user testing, and 6) iterative user testing and redesign of the decision tool prototypes. The final products of this work will be a set of validated and highly detailed design specifications for the Pediatric CSI Risk Assessment Tool(s) and clinical process flow diagrams for evaluating children after blunt trauma.[103, 104] Together, these outputs lay the groundwork for rapidly implementing the tool across the entire clinical spectrum of care for children experiencing blunt trauma.

We will use two methodologies to gather data. We will conduct a prospective observational study of children 0-17 years old who present to the ED for care following known or suspected exposure to blunt trauma regardless of whether or not injuries were sustained. Children will be included if they meet any one of the following: (a) undergoing trauma team evaluation, (b) transported from the scene to site facility by EMS, (c)

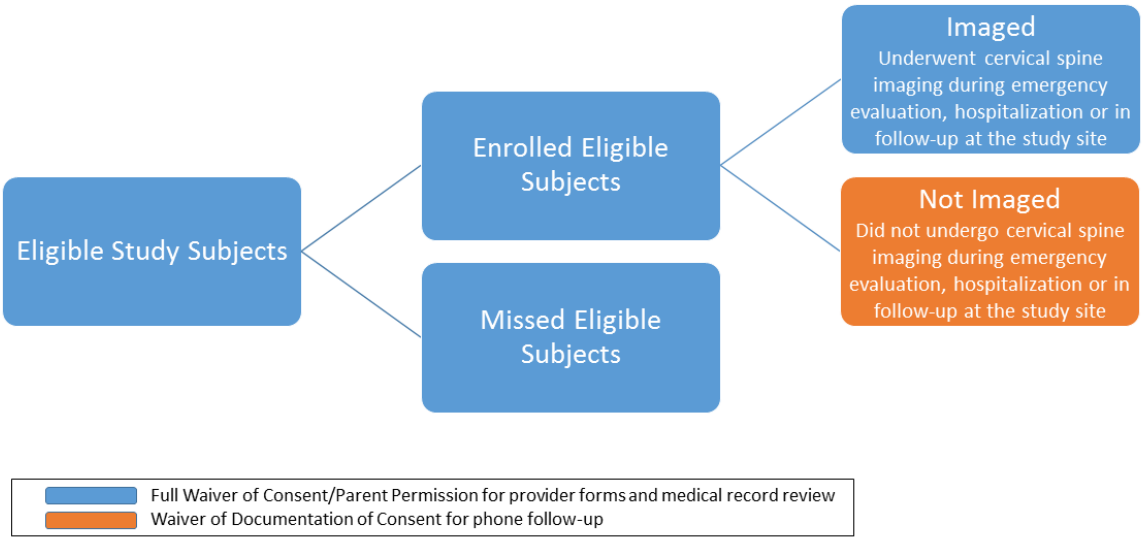


Figure 3: Study Population

undergoing cervical spine imaging at site facility, or (d) transferred to site facility with cervical spine imaging. We will exclude children if they are exposed to a solely penetrating trauma mechanism. Figures 3 and 4 on page 24 represent the study population and study workflow.

CSI, the outcome of interest, is defined as vertebral fracture, ligamentous injury, intraspinal hemorrhage, or spinal cord injury (on either MRI or spinal cord injury without radiographic association) involving the cervical region of the spine (occiput to the 7th cervical vertebra including ligamentous structures attaching the 7th vertebra to the 1st thoracic vertebra). Presence of CSI will be determined by review of study site cervical spine imaging reports and if applicable spine surgeon consultation notes and phone follow-up. At 21 days after the ED visit for injury, the study site medical records will be reviewed for cervical spine imaging and spine surgeon consultation. Children will be considered to have CSI if after cervical spine imaging and if applicable consultation with a spine surgeon; they are determined to have CSI. If imaging report diagnoses conflict with spine surgeon consultation, the treating spine surgeon will be contacted for clarification.

To ensure that there are not missed CSI for those children not undergoing cervical spine imaging, we will review the medical record for follow-up encounters and if necessary, conduct phone follow-up 21-28 days post study enrollment. We will also collect data on patients that are eligible for the study but are not enrolled (missed eligibles).

We estimate that it will require a total observation of at least 22,000 children who are evaluated after blunt trauma to adequately assess our study aims. Enrollment will incorporate a staggered site enrollment plan to allow for an iterative process for the study tool design to meet the study specific aims and objectives. Study objectives include:

1. Develop the Pediatric CSI Risk Assessment Tool in children with blunt trauma using prospective observational data obtained from ED providers; AND

2. Validate the Pediatric CSI Risk Assessment Tool in a separate population of children with blunt trauma using prospective observational data obtained from ED providers; AND

3. Validate the Pediatric CSI Risk Assessment Tool using prospective observational data obtained from EMS providers.

In parallel with the prospective observational study, we will capitalize on the research infrastructure to characterize the clinicians' decision-making relative to screening children for CSI by conducting an Applied Cognitive Task Analysis (ACTA).[105] Task analysis has been applied to system design for nearly 100 years starting with the work of Frederick Taylor's time and motion studies to improve worker productivity.[106] These methods have evolved to the more contemporary cognitive task analysis and now include methods for identifying the cognitive skills or mental demands needed to perform a task proficiently.[105, 107] For our project, we will apply a more streamlined, practical approach to performing a cognitive task analysis, the ACTA, which is based on three basic interview methods designed to produce results that can be applied to system design: task diagram interview, 2) knowledge audit, 3) simulation interview.[105] We will perform each interview method with representative end-users (EMS, ED personnel, and surgical staff affiliated with participating study sites and their affiliated outlying hospitals and agencies) and subject matter experts (i.e. the research team).

Together, the prospective observational study and the ACTA will inform the iterative design of a Pediatric CSI Risk Assessment Tool (Figure 2 on page 18).

# 4 Study Procedures and Data Collection: Prospective Observational Study

Figure 3 on page 19 depicts the study population relative to consent procedures. This study will include the collection of observational data from EMS providers, ED providers, and surgical providers and review of the medical record. These activities will be conducted under waiver of informed consent/parental permission and waiver of authorization. This is a minimal risk prospective observational study with no therapeutic interventions. Legal guardians of patients will be given a Consent, Parental permission, and Authorization cover letter that provides information regarding the study and information that they may be contacted for a brief telephone follow-up observational assessment if their child did not have imaging of their head/neck at time of their child's hospital visit at the study site or it's affiliated facilities.

## 4.1 Subject Identification

Potential subjects will be identified through research staff structured screening of real-time electronic medical records, in particular the ED tracking system. Patients will be screened for eligibility if they present for evaluation after known or suspected exposure to blunt trauma regardless of whether or not injuries were sustained. A screened patient is eligible if the patient meets one of the following criteria: (a) undergoing trauma team evaluation, (b) transported from the scene to site facility by EMS, (c) undergoing cervical spine imaging at site facility, or (d) transferred to site facility with cervical spine imaging. Once a potential patient is identified, the patient will be enrolled in the study as long as they meet the eligibility criteria in Section 1.2.

To identify missed eligible children, we will review the previous day's ED census reports. Children meeting inclusion criteria are screened and general demographic information is obtained.

## 4.2 Study Workflow

Figure 4 represents the study workflow relative to the study population for the prospective observational study. The numbers within the figure correspond to the following study tasks:

1. A patient arrives in the emergency department (ED) by emergency medical services (EMS) or private vehicle.

(a) RC identifies patient: The RC is notified of the potential subject and reviews the patient chart to verify the patient has known or suspected blunt trauma and is being evaluated as described in section 4.1. If the patient meets criteria the RC completes the Screening Form and continues to step 2.

(b) RC does not identify patient: On a regular basis, the RC reviews the ED census reports for potential patients not identified at point of ED arrival/treatment. For patients who meet inclusion criteria, the RC completes the Missed Eligible Form.

2. RC launches the appropriate provider forms for eligible subjects based on patient presentation to the ED.

(a) For patients who arrive by EMS from the scene of the injury: The EMS provider transfers patient care to the ED provider, and is approached by the RC to participate in the study. If the EMS provider agrees to participate, the RC launches the EMS Provider Form for the provider to complete. Once the form is complete, or if the EMS provider declines or is not available to approach, the RC continues to step 3.

(b) For patients who arrive by private vehicle, EMS transfer, or other means: The RC continues to step 3.

3. The ED provider completes the initial physical exam and history on the patient and the RC launches the ED Provider From for the provider to start. If the ED provider confirms the patient is eligible, the observational section of the form is completed and the RC continues to step 4. If the patient is not eligible, the form ends and no further action is required.

4. For eligible subjects, if a surgical provider is available and agrees to participate in the study, the RC launches the Surgical Provider Form for the provider to complete. Once the form is completed, or a provider is not available or does not agree to participate, the RC continues to step 5.

5. For children that did not get imaging: Prior to the patient leaving the ED, the RC provides the family with the Consent, Parental permission, and Authorization cover letter. *Sites will have the option to send this via mail if the RC cannot make contact before the subject leaves the ED.* The RC then completes the Demographics and Disposition Form and the RC continues to step 6.

6. On days 21-28 post ED enrollment, the RC reviews the patient's medical record and completes the Patient Outcome Form. The RC also reviews the chart for cervical spinal imaging and completes the appropriate form.
   (a) If cervical spine imaging is NOT documented in the record: The RC conducts a phone interview and completes the Phone Follow-Up Form.
   (b) If cervical spine imaging is documented in the record: The RC and the PI complete the Imagining/Consultation/Surgery Form.
7. For subjects who had abnormal cervical spine imaging, the study adjudicator completes the Patient Diagnosis Form.

## 4.3 Observational Data

This study will use an electronic tablet system that will be managed by the research coordinator (RC) to gather observational data. The RC will verify patient's inclusion/exclusion criteria based on information available and/or documentation during the time of enrollment through prompted questions. EMS and ED Provider Forms will automatically launch providing observational questions for both providers if the patient is eligible. The RC will be responsible for managing the tablet operated observational data system to verify the correct questions launch and that it is completed by the correct provider.

- ***EMS Providers:*** RCs must verify the correct form has been launched prior to administering the observational assessment to the EMS provider. The form will be available if the patient arrived by EMS directly from the scene of injury and the EMS Provider who provided the patient's assessment is available and willing to fill out form. EMS Providers complete the EMS observational data assessment following the transition of care to the ED providers and prior to leaving the hospital. Once the EMS Provider Form is complete they return the tablet to the RC and returns to service.
- ***ED Providers:*** RCs must verify the correct form has been launched prior to administering the observational assessment to the ED provider. The ED Provider Form should be completed by the ED Provider who performed/or was present during the assessments on the patient to verify eligibility and complete the ED Provider Form. If the patient arrives by private vehicle (or other means), arrives as a transfer from another facility, or does not directly arrive from the scene of injury by EMS the study RC will launch the observational assessment for the ED Provider to confirm patient eligibility and complete the ED Provider Form.

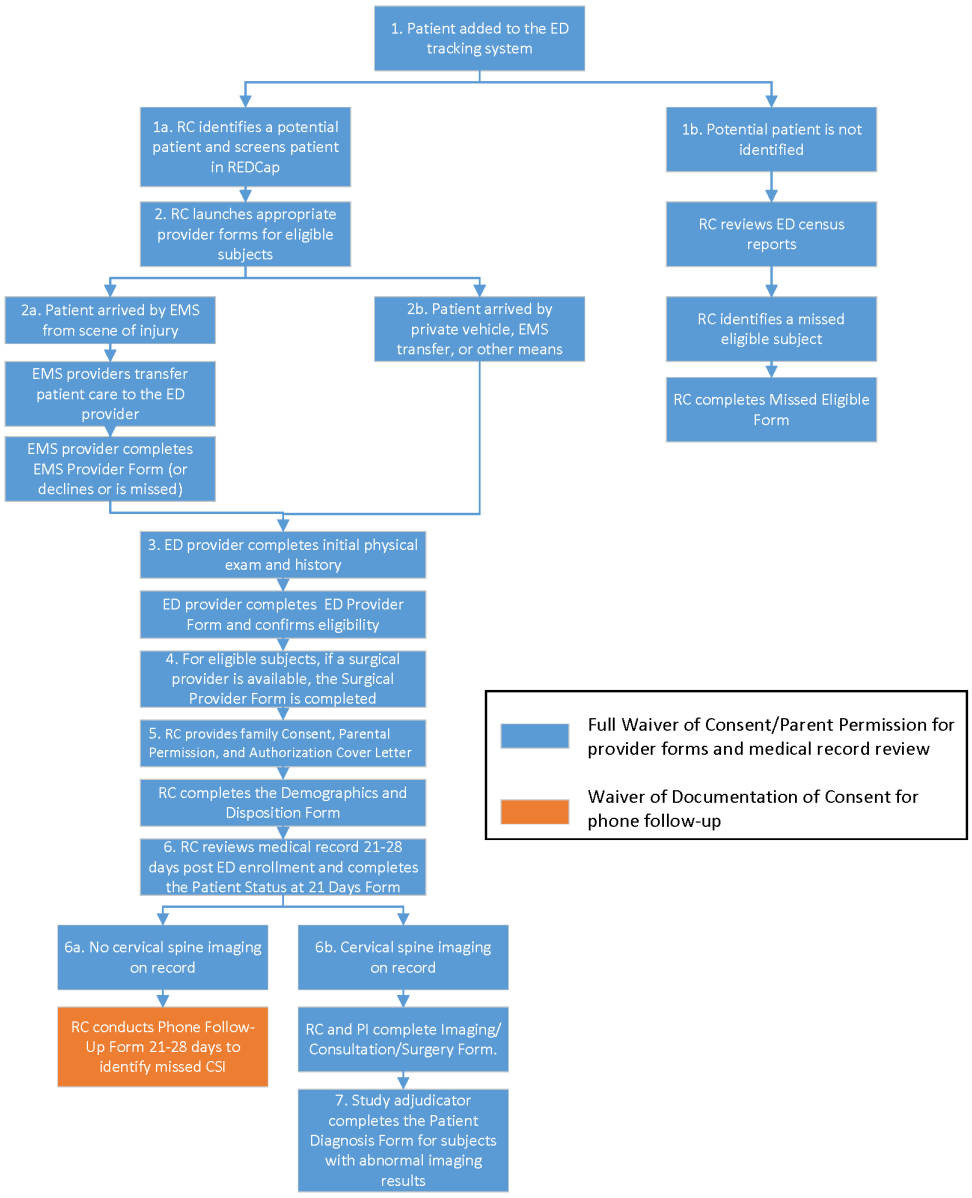


Figure 4: Study Workflow

- ***Surgical Providers:*** RCs must verify the correct form has been launched prior to administering the observational assessment to the Surgical provider. The Surgical Provider Form should be completed by a Surgical Provider who assessed the patient in the ED. Once the Surgical Provider Form is complete they return the tablet to the RC and returns to service.

## 4.4 Follow-up Assessment(s)

Legal guardians of patients who did not get cervical spine imaging will be given a Consent, Parental permission, and Authorization cover letter that provides information regarding the study and information that they may be contacted for a brief telephone follow-up assessment. Patients that do not receive cervical spine imaging at the study site or its affiliated facilities within 21 days of their child's hospital visit, unless the legal guardian refuses, will receive a telephone call assessment from the RC to discuss injury status. Verbal consent will be obtained from a parent or legal guardian to determine if the patient had a delayed diagnosis of cervical spine injury. Assessments must be completed between 21 and 28 days after ED enrollment.

We selected 21-28 days for record review and phone follow-up because previous studies demonstrated that patients' with CSIs missed on their initial visit are usually diagnosed within 3 weeks of injury.[108, 109] PECARN has used this method of identifying missed injuries in previous studies.[92, 96, 97]

## 4.5 Medical Record Review

The research staff will review the patient's medical record to determine eligibility, confirm basic demographic information and determine CSI status. If the RC deems the patient is eligible based on existing documentation, he or she will launch the EMS, ED, or Surgical Provider Forms in REDCap as appropriate. Each study site will have different electronic medical records for patients. The following study forms will be completed through review of the patient's electronic medical record for those who are eligible for the study:

- Demographics and Disposition Form
- Imaging/Consultation/Surgery Form
- Patient Outcome Form
- Diagnosis Form
- PHI Form (site use only)

- Missed Eligible Form (if applicable)

Data will be collected in REDCap. REDCap protects PHI through filters to limit access to site data to the site research team. For example, the PI of the protocol, data manager and the bio statistical team has access to all the de-identified information of participants enrolled. Site-specific research team members only have access to their site's data which are not de-identified. Each study site will use REDCap, and the data will be securely collected at different locations but managed within the same system at the DCC.

## 4.6 Withdrawal from Study

Parents may withdraw their child from participation in the phone follow-up call if applicable. We will not contact the family to collect new information about their child. However, we will use information obtained through prospective observational methods and retrospective chart review as these activities are covered under waiver of informed consent. There are no penalties nor benefits lost to the patient if the legal guardian decides to withdraw their child's data. The RC will notify the DCC of the participants request to have their information removed from REDCap. The DCC data manager will remove the participants data upon receiving a request from the study site's RC.

# 5 Study Procedures and Data Collection: User-Centered Design Activities

In parallel to the prospective cohort study which is aimed at deriving and validating a decision rule, we will perform activities which will inform the design of implementation ready Pediatric CSI Risk Assessment Tool. Participation in ACTA activities are voluntary and participants will be provided a Provider Consent cover letter that explains the activities to be performed. At the time of participation, each participant will be assigned a study identification number. This number will be used on study materials and in the study database instead of names and other private information. A separate list that links each participant's name to the study identification number will be maintained for future reference and communication. Access to this list will be restricted to specific study team members.

Interviews will be audio-recorded. The audio-recordings will be deleted from the recording device immediately after they are saved to computer. Computer files will be stored on a password protected computer system in a secure location. The key linking the participant's name to responses will be removed from the computer system after the

study has closed. An unidentified dataset and back-up copies will remain on an encrypted remote back-up system. The tapes will be reviewed and relevant information transcribed into text. Participant names and any other identifying information will be omitted to assure confidentiality.

## 5.1 Subject Identification

We will rely on information obtained from subject matter experts (the research team) and the tools clinical end-users; EMS, ED personnel, and surgeons that are representative of trauma systems across the U.S. The subject matter experts will be responsible for identifying clinical end-users within their hospitals catchment areas. Table 3 outlines important provider attributes for sampling to ensure that participants are representative of all potential tool users. Our plan is to engage 3-5 clinical end-users per each provider type (clinical end-users), strategically sampling to ensure representation across ED and agency attributes.

## 5.2 Study Workflow

We will engage the subject matter experts and clinical end-users in qualitative and quantitative methods that will be conducted in three phases:(1) Applied Cognitive Task Analysis (ACTA) comprised of three interview activities to capture and represent subject workflow and knowledge; (2) Iterative design where clinical end-users participate in a process of assessing the tool design utilizing mock-ups and formative user testing; and (3) Summative testing where clinical end-users participate in a detailed simulation scenario-based usability testing to validate the tool design. The alignment of these activities with the prospective observational study is illustrated in Figure 5.

### 5.2.1 Applied Cognitive Task Analysis

The applied cognitive task analysis (ACTA) is an established human factors method to describe complex processes in terms of the user task flow, but also cognitive factors such as knowledge, goals and decisions critical to the design of an effective tool. The ACTA consists of three semi-structured interviews to elicit and represent knowledge: (1) Task Diagram. (2) Knowledge Audit. (3) Simulation interview. The task diagram interview will provide an initial presentation of the workflow and cognitive tasks. The knowledge audit will capture details of subject knowledge and expertise. The simulation interview will involve subject responses to complex and challenging patient scenarios. Clinical end-users representing each of the three cohorts will be purposively sampled from each site to participate in these interviews.

| User-Centered Design Subject Sampling Strategy | | | | | | |
|---|---|---|---|---|---|---|
| Emergency Department (ED) Provider Types and ED Attributes | | | | | | |
| Provider Type | Region of US | Urban/Rural Designation | Trauma Center Level-State Designation | American College of Surgeon Verified | Free-standing Children's Hospital | Teaching |
| Emergency physicians (general and pediatric) | Northeast | Large metropolitan (>1 million) | Level I | Level I | Yes | Yes |
| General physicians (internal medicine, family medicine and pediatric) | Midwest | Medium metropolitan (250,000-999,999) | Level II | Level II | No | No |
| General surgeons (pediatric and adult) | South | Small metropolitan (50,000-249,999) | Level III | Level I Pediatric | | |
| Spine surgeons (orthopedics and neurosurgery, pediatric and adult) | West | Micropolitan/noncore (<50,000) | Nontrauma | | | |
| Physician extenders (advanced practice nurses and physician assistants) | | | | | | |
| Emergency Medical Services Provider Type and Agency Attributes | | | | | | |
| Provider Type | Region of US | Urban/Rural Designation | Organizational Structure | Remuneration | Locus of Control | Primary Response Staffing |
| Basic Life Support (BLS) | Northeast | Large metropolitan (>1 million) | Municipal | Volunteer | Local | BLS |
| Advance Life Support (ALS) | Midwest | Medium metropolitan (250,000-999,999) | Contractor | Paid | County | ALS |
| Advanced practice | South | Small metropolitan (50,000-249,999) | | Mixed | State | Mixed |
| | West | Micropolitan/noncore (<50,000) | | | Regional | |

Table 3: User-Centered Design Subject Sampling Strategy

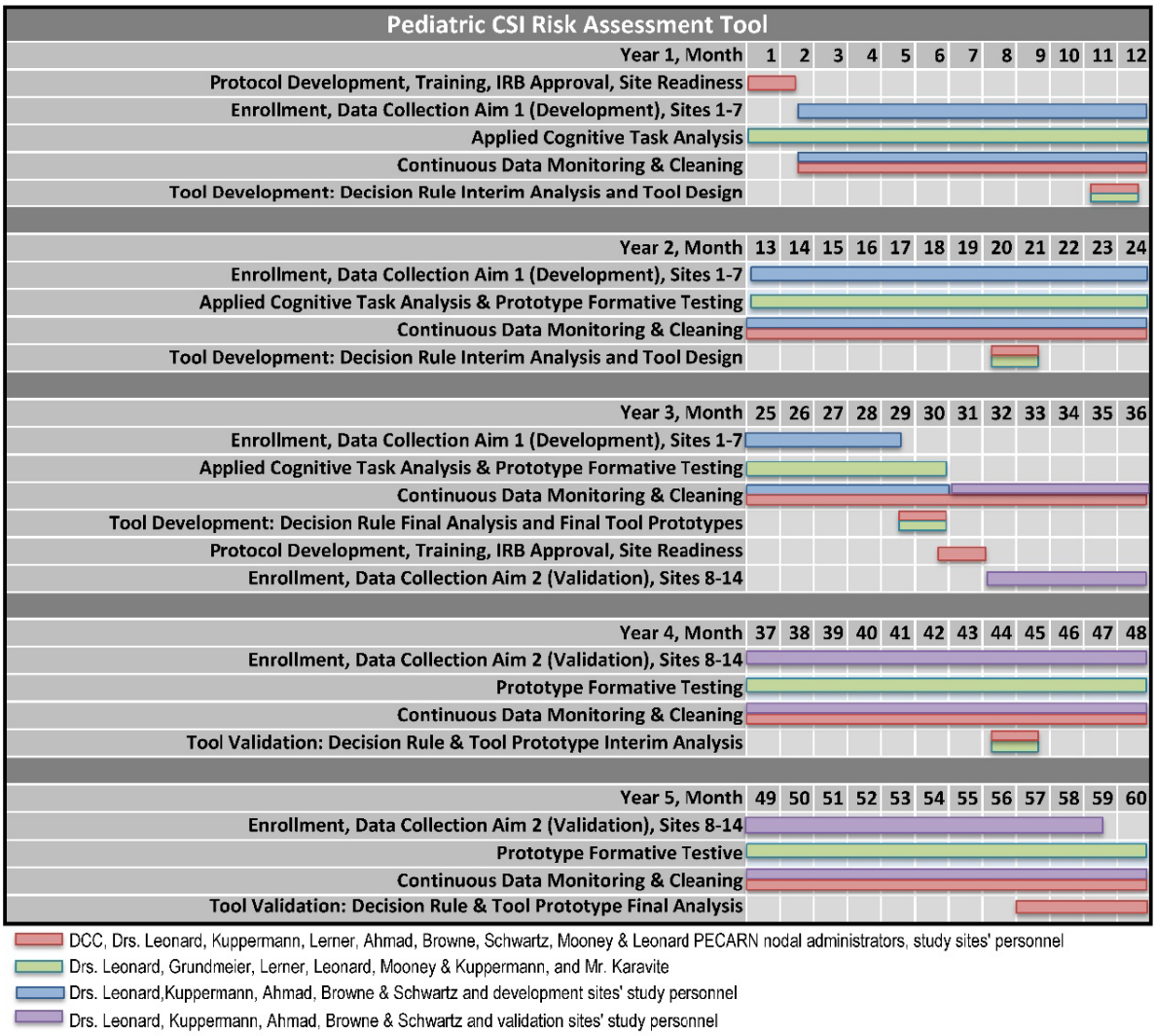


Figure 5: User-Centered Approach Study Workflow

### 5.2.2 Iterative Design

Using the results of the ACTA we will create a set of scenario-based mockups of the tool. In this phase, purposively sampled subjects from each end-user group will react to and provide suggestions regarding tool mockups that will be presented in the context of realistic clinical scenarios. Topics explored will be based on our conceptual model derived from the ACTA for how a CSI tool may improve the process of care and patient outcomes. An iterative process will be used in which the topics discovered will be applied to mockup refinement or redesign and subsequent re-testing until objectives are achieved.

### 5.2.3 Summative Testing

We will conduct a simulation-based usability study in which a purposive sample from each of the three cohorts will attempt to perform a series of tasks with a functioning prototype of the tool. The usability of the system will be assessed quantitatively and qualitatively. Quantitative measurements include task completion, error rate and time on task.

## 5.3 Data Collection Methods/Tools

### 5.3.1 Applied Cognitive Task Analysis

While the content of the three ACTA interviews will differ, and use unique interview guides based on the end-user group, the procedure will be the same. All subjects will receive a Provider Consent cover letter. For each ACTA interview subjects will be instructed on the purpose and format of the interview and will complete a short demographic questionnaire. Subjects will be audio recorded as they respond to open ended questions from the interview guide developed to elicit their knowledge and tasks associated with the diagnosis and treatment of patients with a suspected CSI with the three ACTA interviews sequentially capturing more detailed information. The audio files of the interviews will be reviewed and relevant information transcribed into text.

We will compile the information from all three interview processes into a cognitive demands table which itemizes each difficult cognitive element by relevant end-user, why it is difficult, common errors, and cues and strategies used to avoid errors. The cognitive demands table will help the research team achieve the projects goals by providing them information and requirements that will aid the development of a useable Pediatrics CSI Risk Assessment Tool and content to facilitate the subsequent implementation of the tool into various settings. We will confirm the information obtained during the interviews through questions incorporated into the real-time electronic provider assessment form and structured review of the electronic medical record.

### 5.3.2 Iterative Design

Clinical end-users will be instructed on the purpose and format of the design review. After receiving a Provider Consent cover letter, they will be asked to fill out a short demographic questionnaire. Clinical end-users will then be presented realistic patient scenarios in which a child should be screened for CSI following blunt trauma along with tool mockups related to each patient scenario. At each page or screen of the mockup the clinical end-users will be asked what actions they might perform with the tool (e.g. clicking a particular option or filling in data field). The test facilitator will record whether or not the subject completed the desired actions. At the end of the session the subject will fill out a questionnaire with a series of questions rating the functionality, usability and utility of the tool. All data from these sessions will be entered into a Redcap database using the subject's identification number.

The results of the testing sessions will be applied to refining or redesigning the mockups and the user testing procedure will be repeated. This entire process will be iterated until satisfactory results of the mockups are obtained. We estimate a set of three iterations will be performed.

### 5.3.3 Summative Testing

Clinical end-users will be instructed on the purpose and format of the simulation-based usability test, will receive a Provider Consent cover letter and will complete a short demographic questionnaire. Realistic patient scenarios will once again be used and presented. It will be stressed to each subject that the purpose of the review is to evaluate the system and not the users' capabilities, and that any difficulties discovered in the test will reveal issues with system design, not the subject's skills or competency. The evaluation will be based on a mix of qualitative and quantitative data as they interact with the tool prototypes via patient scenarios. This data will be used to assess three primary aspects of the tool. (1) Support decision making. (2) System utility. (3) System usability. Though we anticipate the Formative Design phase will address any serious defects, if initial testing reveals issues that are consistent and severe, we will modify the prototype and test the changes with new subject. We will confirm the information obtained during the interviews through questions incorporated into the real-time electronic provider assessment form and structured review of the electronic medical record.

## 5.4 Withdrawal from Study Activities

Subject matter experts and clinical end-users may withdraw from participation in user-centered design activities at any time without prejudice to their employment status. It

will be documented whether or not each subject completes the study.

# 6 Study Procedures and Data Collection: Diversity Supplement

## 6.1 Diversity Supplement Study Summary

This diversity supplement will build off a currently enrolling multi-center prospective observational study of children who have sustained blunt trauma and may be at risk of cervical spine injury (CSI). The investigators of the parent study aim to develop and test a pediatric cervical spine injury risk assessment tool that can be used by EMS and ED providers to determine which children warrant spinal precautions and cervical spine imaging after blunt trauma. Addressing the social factors to reduce health inequities is a global health care priority, but the nature of their association with pediatric treatment and outcomes of CSI remains unstudied. We propose to expand the aims of the parent grant by examining social factors with hypothesized CSI care associations in the patients and families who are enrolled in the current study. Our study is significant because it aims to identify modifiable health care disparities that can be reduced through targeted interventions.

## 6.2 Diversity Supplement Specific Aims

Our study aims to identify modifiable health care disparities that can be reduced through targeted interventions and has the Specific Aims below:

- Specific Aim 1. Determine social factors associated with pediatric CSI risk using census tract data from the American Community Survey and other geographic data.
- Specific Aim 2. Determine social factors affecting disparities in health care delivery, post-injury care management, and functional outcomes in children with CSIs via structured interviews.

## 6.3 Diversity Supplement - Subject Eligibility, Accrual and Study Duration

Eligible participants will be identified by study staff. Patients will be enrolled in the study if they meet the following inclusion criteria:

- Enrolled in the parent grant and has a CSI as determined by the study neurosurgeon

CSI, the outcome of interest, is defined in the parent grant as vertebral fracture, ligamentous injury, intraspinal hemorrhage, or spinal cord injury (on either MRI or spinal cord injury without radiographic association) involving the cervical region of the spine (occiput to the 7th cervical vertebra including ligamentous structures attaching the 7th vertebra to the 1st thoracic vertebra). Presence of CSI will be determined by review of study site cervical spine imaging reports and through applicable spine surgeon consultation notes and phone follow-up. Children will be considered to have CSI if after cervical spine imaging and if applicable consultation with a spine surgeon; they are determined to have CSI. If imaging report diagnoses conflict with spine surgeon consultation, the treating spine surgeon will be contacted for clarification.

Our study will enroll all pediatric patients diagnosed with CSI identified in the parent grant for medical record review and will attempt telephone follow-up survey for each patient during the 24-month enrollment period of the supplement. The parent grant will identify at least 360 pediatric patients diagnosed with CSI following blunt trauma. Based on prior studies using similar methodology, we expect that at least half of these families will agree to participate in the follow-up survey.

## 6.4 Diversity Supplement - Rational and Background

Injury is the leading cause of morbidity and mortality in children, and there are vast disparities within childhood trauma that are both multifactorial and poorly understood.[110] Furthermore, there is a paucity of literature regarding the social factors related to pediatric cervical spine injury risk. The evidence for disparities within pediatric trauma patients is sparse and incomplete within the literature1. Elucidating the specific social factors that are related to CSI risk and poor outcomes has the potential to inform new strategies in prevention and post-injury interventions for at-risk youth. Although pediatric CSIs are uncommon events, over 1300 new cases occur every year and the injuries contribute to significant morbidity and mortality.[111, 112] Examining the role of social factors in pediatric CSI will fill two major gaps in the present literature: (1) While there is considerable evidence of racial and ethnic health disparities in the adult trauma literature,[113–116] little is known about such disparities in children or about how social factors contribute to pediatric CSI risk and outcomes. African-American children have been independently identified as having increased morbidity, mortality and functional deficit after traumatic brain injury compared to equivalently injured Caucasian children.[116, 117] Although these studies clarify the relationship between trauma and disparities in general, the focus of the studies was not pediatric CSI. (2) There is a paucity of literature that addresses the disparities in health care delivery and functional outcomes in children with CSIs. To our

knowledge, no researchers have prospectively examined how social factors are associated with pediatric cervical spine post-injury care and functional outcomes.

## 6.5 Diversity Supplement - Overall Study Design

The proposed research will investigate how social factors are associated with pediatric cervical spine injury (CSI) risk, post-injury care and functional outcomes. Our project will use two methodologies to gather data: (1) retrospective review of the electronic medical record and structured medical billing data prepared for the Pediatric Health Information System (PHIS) and (2) fixed-response telephone-administered questionnaire. The final products of this work will lay the groundwork for future studies to create targeted interventions for injury prevention and health care facilitation to improve functional outcomes for at-risk youth.

Children will be included if they were enrolled in the parent grant and sustained a CSI as confirmed by the study neurosurgeon. From the parent study, we will be able to obtain information about the type of CSI diagnosis and acute care interventions as related to the CSI. Our study will conduct an extended chart review for pediatric CSI patients to richly describe social factors present in CSI patients, to further ascertain acute care intervention information and resources at the time of discharge. Additionally, we will also request PHIS IDs to review medical billing data for the incident visit and any subsequent visit within 30 days of the incident visit. PHIS includes patients from over 45 children's hospitals, to which all study sites in the parent grant participates. We will compare CSI patients with the overall population of children in the United States (US) by utilizing census data. Census tract data will be obtained from the American Community Survey. We will retrieve the home zip code at the time of injury for each patient and link in several secondary data sources to capture the social and physical characteristics of the neighborhood/community environment.

In parallel, we will use validated survey tools to assess social factors, health care delivery and functional outcomes of children with CSIs. The child's parent or legal guardian will be contacted via telephone to participate in a fixed-response telephone-administered questionnaire. Social factors will be assessed utilizing the Protocol for Responding to and Assessing Patient's Assets, Risks and Experiences (PRAPARE) and functional outcomes will be assessed through the National Institutes of Health Common Funds Patient-Reported Outcomes Measurement Instrument System (PROMIS) tool. Healthcare utilization and needs will be assessed based on health care services received in the cognitive, physical and socioemotional domains by standardized responses adapted from National Health Interview Survey. Phone calls will be made at least 1 month after initial diagnosis. The time since injury will be collected and included in the analysis. The

surveys are expected to take 15 minutes, and families will receive monetary compensation for participation. We will also include in the analysis retrospective data collected during Aim 1 chart review that includes acute care interventions and discharge resources.

**Diversity Supplement** The activities for Aim 1 will be conducted under waiver of consent and the activities for Aim 2 will be conducted under waiver of written documentation of consent. This is a minimal risk retrospective chart review study with no therapeutic interventions. Legal guardians of eligible subjects will be given a Consent, Parental permission, and Authorization cover letter that provides information regarding the study and information that they will be contacted for a telephone follow-up observational assessment if their child sustained a CSI.

## 6.6 Diversity Supplement - Subject Identification

Subjects for this study will be identified using resources from the parent grant. The eligibility criteria, data collection activities and consent methodologies for each aim are explained below.

- Aim 1. Children with CSI will be identified by the parent grant Data Manager (reference Section 1.2 of the parent grant eligibility criteria). The Data Manager will provide each participating site a list of subject ID's for those children with CSI. These will be the subjects for which we perform a limited chart review and request PHIS participant ID's.

- Aim 2. Subjects from Aim 1 that are conversant in English or Spanish will receive a Consent and Authorization Cover Letter from the study management team at the DCC. This list of subjects will be sent to a limited group of study personnel at Nationwide Children's Hospital (Dr. Leonard, Dr. Wells and a research coordinator (RC)). If a legal guardian contacts the study management team at the DCC to opt out, they will not be contacted by the team at Nationwide Children's for the telephone follow-up. Figures 6 and 7 represent two consent methodologies for the study

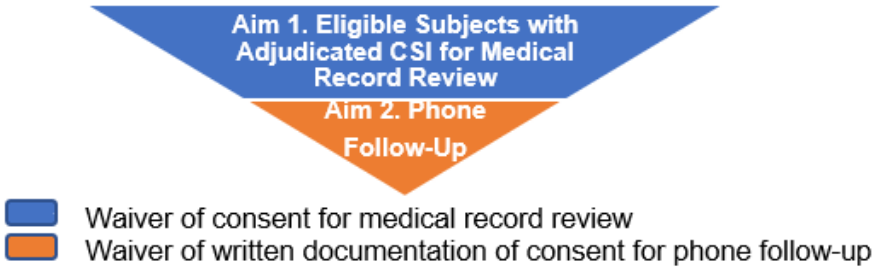


Figure 6: Consent Procedures for Study Population

## 6.7 Diversity Supplement - Study Workflow

This study contains two data collection methodologies conducted under separate consent procedures based on the respective specific aim.

Aim 1. Medical Record Review conducted under waiver of consent

- The parent grant Data Manager will identify subjects with adjudicated CSI.
- The research staff at each study site will perform a limited medical record review for subjects with adjudicated CSI and provide the requested PHIS ID's for the incident visit and any visit within 30 days of the incident visit.

Aim 2. Telephone Follow-up Assessment conducted under waiver of written documentation of consent

- Based upon the limited medical record review, parents/guardians conversant in English or Spanish will be eligible to receive a cover letter.
- The DCC will mail consent the Consent, Parental permission, and Authorization cover letter to the family.
- Eligible parents/legal guardians who are sent a cover letter will be contacted at least 30 days post-ED enrollment by Dr. Wells or RC to complete the Phone Consent form unless the parent/legal guardian chose to opt out.

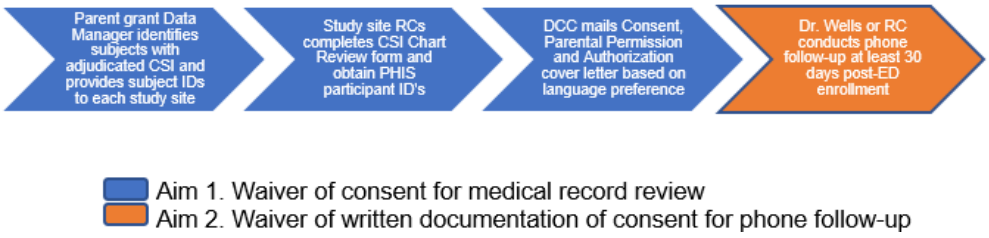


Figure 7: Study Workflow and Consent Procedures

## 6.8 Diversity Supplement - Medical Record Review

The parent grant Data Manager at the Data Coordinating Center (DCC) will identify eligible subjects based on CSI adjudication. They will provide a list of participant ID's for eligible subjects to each study site. The site will complete a supplemental demographic form (limited medical record review) and submit the PHIS ID's to REDCap. All participating study sites prepare and submit billing data to PHIS.

Each study site will use REDCap, and the data will be securely collected at different locations but managed within the same system at the DCC. REDCap protects PHI through filters to limit access to identifiable information. For example, only key study personnel (study PI and parent grant Data Manager) and site-specific research team members only have access to their site's data which are not deidentified. Data management for PHIS medical billing data will be conducted centrally at Nationwide Children's Hospital, the lead study site, by the Nationwide Children's Hospital PHIS Data Manager. For the medical billing data, patient encounters will be assigned a unique study identification number by PHIS that will be associated with the study participant number. A deidentified dataset will be used for statistical analyses. The electronic data will be deleted within seven years following the last publication stemming from the study.

## 6.9 Diversity Supplement - Telephone Follow-up Assessment

Legal guardians of patients with CSI who have been identified as conversant in English or Spanish will be mailed a Consent, Parental Permission, and Authorization Cover Letter. This cover letter provides information regarding the study and information that they will be contacted for a telephone follow-up assessment. This cover letter will also include instructions for how to opt out of telephone follow-up. Unless the legal guardian has contacted the Project Manager at the DCC and elected to opt out of the telephone follow-up, they will receive a phone call from either Dr. Wells or a RC at least 30 days after

ED enrollment into the parent study. At the beginning of this call, the interviewer will explain the study and obtain verbal consent. At this time, the legal guardian can decline participation or continue with the phone interview. If participation in the phone interview is declined, all subsequent attempts for contact and recruitment will be terminated. If the legal guardian consents to participation, the interviewer will administer a structured questionnaire that assesses the patient's demographics, functional outcome, resources needed upon discharge and ongoing healthcare needs.

If initial telephone attempts to contact the legal guardian are unsuccessful, subsequent attempts will be limited to three total attempts. If voicemail is encountered, we will leave a message and callback information for the legal guardian to assist with arranging follow-up. If the telephone number is a disconnected line, all subsequent attempts for contact to that telephone number will be terminated. Our final attempt to contact a family for telephone follow-up will be a mailed letter notifying them that attempts to contact for participation in the survey had been made, provide contact information should they want to participate and confirm no further contact will be attempted.

For time and inconvenience, legal guardians will receive $50.00 for completing the phone interview. Funds will be issued on a debit card specially designed for clinical research, ClinCard. The ClinCard Research Stipends Payment System is designed to deliver electronic payments to program participants for time associated with clinical trials. In order to process the payment, we will need to verify their mailing information, patient's name and date of birth, legal guardian's name, and telephone number. When the interview is completed, funds will be approved, automatically loaded onto the card and mailed to the legal guardian's home address.

We selected 30 days for telephone follow-up because previous studies demonstrated that patients with CSI missed on their initial visit are usually diagnosed within 3 weeks of injury.[108, 109] PECARN has used this method of identifying missed injuries in previous studies.[92, 96, 97] Additionally, a benchmark for care per the Centers for Medicare and Medicaid Services is the 30-day readmission rate, therefore we plan to gather information within 30 days of the initial ED visit. Finally, this would give enough time for eligible subjects in the parent grant to complete the adjudication process for CSI.

## 6.10 Diversity Supplement - Withdrawal from Study

Parents may withdraw their child from participation in the telephone follow-up. We will not contact the family to collect new information about their child if they opt out or ask to withdraw from the telephone follow-up. However, we will use information obtained through prospective observational methods (see 4 in parent grant) and retrospective chart review as these activities are covered under waiver of informed consent. There are no

penalties nor benefits lost to the patient if the legal guardian decides to withdraw their child's data.

## 6.11 Diversity Supplement - Data Analysis

This study has two methodologies for data analysis based upon the specific aims.

- Specific Aim 1. Determine social factors associated with pediatric CSI risk using census tract data from the American Community Survey and other geographic data.

  Standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentage for categorical variables such as gender) will be used to summarize demographic variables. To analyze whether the distribution of social factors in the CSI population differs from that in the general population we will calculate a standardized incidence ratio based on population level data from the American Community Survey. The methodology compares the observed distribution of social factors in the study's CSI population to what would be expected in the general population based on a synthetic cohort from census data.

- Specific Aim 2. Determine social factors affecting disparities in health care delivery, post-injury care management, and functional outcomes in children with CSIs via structured interviews.

  Univariate analysis using chi-square testing and multivariate logistic regression will be used to determine the association between social factors and inequities in healthcare delivery and functional outcome for children with CSI including school performance, accessibility of healthcare resources, ED visits, and unplanned readmissions.

## 6.12 Diversity Supplement - Consent Procedures

This study has two methodologies for consent procedures based upon the specific aims.

Aim 1. Medical Record Review  Waiver of Consent Process

We are requesting a waiver of consent based on the following qualifications: the research is limited to existing data; the data involves no more than minimal risk to the subject; waiver of consent will not adversely affect the rights and welfare of subjects,

and the research could not be practicably carried out without the waiver. The proposed study meets all regulatory requirements for a waiver, as outlined in the Code of Federal Regulations Title 45 Part 46, "Protection of Human Subjects". Justification is provided below.

- See 45 C.F.R. 46.116 (d)(1) See 10.4 The research activity proposed in this application is retrospective chart review and minimal risk.
- See 45 C.F.R. 46.116 (d)(2) See 10.4 Beyond medical record review, there are no activities or interventions outside of routine clinical care. Nothing proposed in the research will adversely affect the rights and welfare of the subject.
- See 45 C.F.R. 46.116 (d)(3) See 10.4 The research proposed in this application would be impracticable to conduct if informed consent is required. Eligible subjects enrolled in our study are identified through the parent grant which currently operates with a waiver of informed consent. In addition, PHIS data sets are derived from over 45 hospitals throughout the United States; therefore, data collection and reporting would not be feasible if the waiver of HIPAA authorization was not carried out. We are requesting a waiver of HIPAA authorization based on the following qualifications: the use or disclosure of PHI involves no more than minimal risk, the research could not practicably be conducted without the waiver or alteration, and the research could not practicably be conducted without access to and use of PHI. The protected health information will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of the research project.
- See 45 C.F.R. 46.116 (d)(4) See 10.4 The research activity proposed in this application is retrospective chart review, so no additional pertinent information will be provided to the subjects.

Aim 2. Telephone Follow-up Assessments Waiver of Written Documentation of Consent

We are requesting a waiver of written documentation of consent. The proposed study meets all regulatory requirements for a waiver, as outlined in the Code of Federal Regulations Title 45 Part 46, "Protection of Human Subjects". Justification is provided below.

- **21 CFR 56.109(c)(1) and 45 C.F.R. 46.117 (c)(1)(ii) Research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.**

The research activity proposed in this application is a telephone interview which is a minimal risk activity. Beyond the interview, there are no activities or interventions outside of routine clinical care.

- See 45 C.F.R. 46.116 (d)(1) See 10.4 The research activity proposed in this application is retrospective chart review and minimal risk.
- See 45 C.F.R. 46.116 (d)(2) See 10.4 Beyond medical record review, there are no activities or interventions outside of routine clinical care. Nothing proposed in the research will adversely affect the rights and welfare of the subject.
- See 45 C.F.R. 46.116 (d)(3) See 10.4 The research proposed in this application would be impracticable to conduct if written informed consent is required as eligible subjects are recruited through a national, multi-center trial study across the country for telephone follow-up assessment.
- See 45 C.F.R. 46.116 (d)(4) See 10.4 Guardians of eligible children will be provided a Consent, Parental Permission, and Authorization Cover Letter from the DCC regarding the study. This handout will be mailed to the legal guardian's home address if the legal guardian is conversant in English or Spanish languages. A follow-up call will be made to the legal guardian. At the time of the phone call, Dr. Wells or RC will confirm that the legal guardian has received the cover letter and obtain verbal consent for the phone follow-up questions.

Figure 6 represents the proposed research activity and respective requested waivers of consent for the study population

# 7 Data Management

We will collect data using structured observational assessment forms regarding factors that have been shown previously to be associated with risk for CSI in children.[90] Relevant data will be collected by two methods: (1) Electronic questionnaires using tablets and wireless technologies during the visit and (2) Detailed demographic and clinical information from the medical records will be extracted at each institution. This information will be integrated using an existing informatics infrastructure at the DCC.

The RCs will administer the observational assessment forms to the EMS, ED, and surgical providers through a secure web-based, public interface to the data management system via a tablet. The real-time data entry increases the time for review and data analysis and potentially reduces missed or erroneous responses. The electronic version

of the observational assessment forms will be available using a tablet, offering these advantages: (a) improved data quality and completeness by providing safeguards against question omission and inconsistent response; (b) skip patterns and algorithms will be programmed to customize the next questions asked based on previous answers; (c) elimination of manual data entry errors since the data will be transmitted wirelessly and automatically incorporated into REDCap, web-based clinical database management system; (d) a user-friendly and engaging touchscreen interface; and (e) restricts access to PHI. Using REDCap, the data will be securely collected at different locations but managed within the same system.

REDCap is a web-based application designed to support data capture for research studies, providing:

- user authentication and role-based security
- collaborative access to data across academic departments and institutions
- intuitive electronic case report forms (CRFs)
- real-time data validation, integrity checks and other mechanisms for ensuring data quality (e.g. double-data entry options)
- data attribution and audit capabilities
- protocol document storage and sharing
- central data storage and backups
- data export functions for common statistical packages
- data import functions to facilitate bulk import of data from other systems

# 8 Data Analysis

**Tool Development and Evaluation** Figure 2 on page 18 illustrates the iterative process of tool development and validation. This process relies on continuous monitoring of clinical data with interim analyses to model and evaluate potential decision rules in parallel with the Applied Cognitive Task Analysis which will inform the design of the Pediatric CSI Risk Assessment Tool prototypes. We will evaluate the study progress and data collection at multiple time points during the study collection period. The data analysis will use interim evaluations to measure progress towards achieving the study

specific aims. This process of refinement will use qualitative and quantitative methods to solicit input regarding the tool attributes from subject matter experts and clinical end-users, in particular practicing EMS, ED, and surgical personnel.

## 8.1 Specific Aim Analyses

**Specific Aim 1.** Develop the Pediatric CSI Risk Assessment Tool in children with blunt trauma using prospective observational data obtained from ED providers.

The first step in tool development is the refinement of the original PECARN model into a decision rule that has very high sensitivity for identifying CSI in children with blunt trauma and sufficient specificity to result in a meaningful reduction in the use of spinal precautions and radiographic imaging. To evaluate Aim 1 we will use the prospective observational data obtained from ED providers to refine a clinical decision support tool that has near perfect sensitivity (lower 95% confidence limit >95%) and adequate specificity to reduce unnecessary interventions (lower 95% confidence limit >40%) when screening children for CSIs. To develop the decision rule, we will use binary recursive partitioning on a study population consisting of approximately 13,333 subjects collected from eight PECARN sites.

We will use multiple analytic techniques to refine the decision rule that will serve as the basis for the Pediatric CSI Risk Assessment Tool. We will use both CART 7.0.0 (San Diego, CA) to perform recursive partitioning for the purpose of building a clinical decision tree and multivariable logistic regression modeling using SAS 9.4 (Cary, NC) to develop a risk model. This is important because each method will result in a tool that has different characteristics. As an example, we will use regression analysis if we determine that the optimal tool is a "risk calculator" in which a child's risk for CSI is calculated based on the child's individual constellation of findings and guidance for CSI evaluation (e.g. nothing versus plain radiographs versus CT) is set for various risk thresholds. We can use regression analysis, as was performed in our pilot work, to determine a set of variables that has sufficient performance characteristics for use as a simple tool in which the presence of any one finding would identify the child as at non-negligible risk for CSI and therefore requiring further evaluation.[90, 94, 95] Recursive partitioning results in a clinical decision tree in which the resultant tool is a patient care algorithm, with each terminus resulting in a risk estimate on which we base clinical decisions regarding CSI evaluation.[96, 97] Our ACTA will help determine which type of tool and therefore which analytic techniques for decision rule refinement will be most useful for tool design. It may be that ultimate implementation requires multiple different tools based on various patient scenarios which differ by parameters such as setting, provider type, point of entry into the health care system, and timing within the patient's clinical course.

Using the results of our ACTA, we will develop conceptual prototypes of the Pediatric CSI Risk Assessment Tool suitable for user testing. We will perform a series of iterative formative usability tests to evaluate the tool prototypes.[118–120] Prototype assessment will be scenario-based and designed to address the various clinical roles and workflows. At each iterative testing period, we will assess the prototypes in terms of usability, utility and effectiveness, but also in supporting the desired outcome of the decision rule. We will modify the prototypes, or if necessary redesign and retest to address the results. With each iteration, the prototypes will increase in the level of detail and functionality they represent. The development and user testing of conceptual system prototypes is well-established in general usability science and moreover in the development of health information technology solutions.[103, 104, 118, 121, 122] Team members have experience using dedicated software, such as Axure (Axure Software Solutions, San Diego, CA) to support rapid, interactive prototyping of clinical decision support systems suitable for user testing.[123–126]

We will include all children that present to the study site EDs, regardless of point of entry into the health care system. While this is important in terms of building a tool that is representative of the full spectrum of children with CSI, this has the potential for resulting in ascertainment bias on the part of the ED providers responding to the assessment forms. In order to address this potential bias, we will determine the operating characteristics of our prediction tool for the entire cohort as well as key sub-samples of children, including those without cervical spine imaging prior to presentation at the study site, those who do not have a trauma team activation, those who arrive via scene response EMS, and those who arrive via private motor vehicle. For any subgroup with poor performance, we will conduct an exploratory analysis by deriving separate rules. As a standard quality measure for observational studies such as this, we will compare the demographic characteristics of enrolled children to those that were eligible and not enrolled.

In addition, when conducting our analyses, we will examine the operating characteristics of the prediction rule for several high-risk groups including young children (<8 years), children with injuries that require either surgical stabilization or stabilization with an orthotic device for >30 days, children with medical conditions that predispose to CSIs and children who are victims of abusive trauma. For any high-risk group with poor performance, we will conduct an exploratory analysis by deriving separate rules.

While every effort will be made to ensure data quality, we will conduct several analyses to assess the effect of the quality of the data. CART automatically selects surrogate variables in the event that a splitting variable has a missing or unknown value. For regression modeling, we will use multiple imputations to allow for inclusion of records where the provider failed to assess the patient for the clinical finding. Further, if a risk factor in the tool has low prevalence or poor kappa for EMS-ED and ED-Surgical

provider paired observations(lower 95% confidence interval <0.4), the analyses will be re-run excluding the variables for comparison.

**Specific Aim 2.** Validate the Pediatric CSI Risk Assessment Tool in a separate population of children with blunt trauma using prospective observational data obtained from ED providers.

To validate the Pediatric CSI Risk Assessment Tool, we hypothesized that the Pediatric CSI Risk Assessment Tool will retain adequate sensitivity (lower 95% confidence limit >95%) and specificity (lower 95% confidence limit >40%) in an independent sample of children presenting for to the ED evaluation following blunt trauma. To evaluate this aim, we will enroll patients from PECARN sites not involved in enrollment for Specific Aim 1. Using a population of 8,889 collected from the prime site and an additional seven different PECARN sites and the prime, we will report standard performance measures to describe the accuracy of the rule: sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios. We will also report 95% CIs for all above measures. In addition to evaluating the validity of the decision rule, we will continue to perform and report formative testing on the Pediatric CSI Risk Assessment Tool prototypes. If performance of the rule or provider acceptance is low at our interim analysis, we will return to the training set in Aim 1 and approach refining the decision rule using a different process and revalidate. We will report the demographic characteristics of the validation study cohort using means and medians as appropriate for continuous measures and frequencies and percentages for categorical measures.

**Specific Aim 3.** Validate the Pediatric CSI Risk Assessment Tool in a population of children with blunt trauma using prospective observational data obtained from EMS providers.

Using a set of patients who have data from both EMS and ED providers collected throughout the both the derivation and validation phases of the study we will evaluate the performance of the rule using EMS variables. Additionally, we will assess agreement between EMS and ED providers using the kappa statistics. It is expected that there will be a minimum of 7,444 subjects with data from both EMS and ED providers available for this aim. As in Aims 1 and 2 we will report the decision rules performance based on standard measures: sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios. We will also report 95% CIs for all above measures. If performance of the rule derived in Aim 1 is poor we will derive an EMS specific rule using similar methods described above.

# 9 Study Training

## 9.1 Study Training

A formal training program for investigators and research staff will be held prior to the start of enrollment. The training program will cover regulatory topics and review the National Institutes of Health (NIH) required Good Clinical Practice standards. The training will also provide in depth explanations regarding study procedures, clinical care, data entry procedures, quality assurance, and site monitoring procedures. Upon return to their home site, each investigator and research coordinator will train the remaining study staff at their site on the protocol and all research-related duties and functions. Documentation of this training will be required by the PI prior to any site being allowed to initiate the study. A manual of operations will be provided to each investigator prior to the start of enrollment. The manual will detail specific information about the study procedures, regulatory information, protection of human research subjects, and other necessary information. Updates and revisions to the manual will be made available electronically. The Data Coordinating Center, in collaboration with the study investigators will be the main contact for study questions.

## 9.2 Study Monitoring

The investigators recognize the importance of ensuring data of excellent quality. Study monitoring is critical to this process. Monitoring has been a very effective tool for maintaining data quality in previous Pediatric Emergency Care Applied Research Network studies, and we will utilize this process to ensure excellent quality data in the proposed study. The DCC utilizes risk-based methodology to identify and correct problems that may arise at sites. The risk-based approach to monitoring focuses on oversight activities and preventing or mitigating key risks to data quality, as well as to processes critical to human subject protection and integrity of the trial or study.

Study monitors must be provided with appropriate access to study materials and the medical records for study subjects. If the medical records are in electronic form, the clinical investigator or an authorized individual must provide any assistance necessary to facilitate the study monitor's review of data in the electronic medical record.

### 9.2.1 Site Monitoring Plan

A supplemental study-specific risk-based monitoring plan, separate from the protocol will be completed which outlines specific criteria for monitoring. This plan may include the number of planned site visits, criteria for focused visits, additional visits or remote

monitoring, a plan for chart review and a follow up plan for non-compliant sites. The monitoring plan also describes the type of monitoring that will take place (e.g., sample of all subjects within a site; key data or all data), the schedule of visits, how they are reported and a time frame to resolve any issues found.

# 10 Protection of Human Subjects

**Human Subjects Involvement, Characteristics, and Design:** This is a prospective observational study of children who have sustained blunt trauma. The proposed population was selected as it represents the population of children who may be at risk for CSI and in whom there are not clinical guidelines for evaluation and management. We will be observing the cohort of children younger than 18 years old who present to the 18 Pediatric Emergency Care Applied Research Network (PECARN)-affiliated Emergency Departments for evaluation following blunt trauma. In addition, participants must have one of the following: transported from the field by EMS using spinal precautions, undergoing trauma team evaluation, or undergoing cervical spine imaging to evaluate for potential CSI (includes patients transferred with imaging). Our goal is to enroll 22,222 consecutive patients to meet the specific aims of our study. Given the rarity of CSI in children, approximately 18 performance sites are necessary in order to establish the cohort within our specified timeframe. All key personnel involved in conducting the research will receive required education on the protection of human research participants prior to engaging in the research; this includes good clinical practices, human subjects protection and Health Insurance Portability Accountability Act (HIPAA) training. Institutional Review Board approval will be obtained prior to initiating the study.

## 10.1 Institutional Review Board (IRB) Approval

A central IRB (cIRB) at the University of Utah will be used for this study. The Data Coordinating Center will track IRB approval status and will not permit subject enrollment without documentation of initial IRB approval and maintenance of that approval throughout subsequent years of the project.

## 10.2 Potential Risks

The risk to the subjects that participate in this study is the loss of privacy or confidentiality through accidental disclosure of private health information. The aforementioned safeguards will be implemented to protect against this potential risk. Due to these precautions, the likelihood of a loss of privacy or confidentially is minimal.

### 10.2.1 Improper Disclosure of Medical Information

The data will be obtained from up to six sources: treating EMS prehospital provider, treating ED provider, treating Surgical provider (which can include trauma surgeon or spine surgeon), medical record and legal guardian. No biological specimens will be obtained in this study. We will maintain the paper subject records for at least three years after the last Federal Financial Report is submitted to the National Institute of Health.

### 10.2.2 Medical Risks

There are no known or anticipated additional medical risks from participating in the trial.

### 10.2.3 Protections Against Risk

Research Personnel who will have access to identifiable private information are the research personnel (a site principal investigator and their authorized research staff (RCs/RAs) at the study site where the subject was enrolled. Data collection will be electronic; using password protected computing devices that wirelessly transmit data to a secure network drive. These devices will be kept in locked cabinets, in locked suites when not in use. Each subject will be assigned a unique patient identifier for purposes of analysis, and this will be used to link any paper records to an electronic research record within the analytic database. Study site personnel will be responsible for entering the data through the electronic interface into a secure, web-based data management system hosted at the PECARN DCC; thus, the analytic database will be maintained in a secure encrypted HIPAA compliant computing system. Most research results will be presented in aggregate fashion. HIPAA identifiers will be stripped from findings that reference individual subjects. While the majority of the data will be stored electronically, there is a chance that we will need to retain some information on paper records. All paper research records with patient identifiers, if any, will be kept at the site from which they were obtained in locked cabinets, in a locked office, within a locked office suite. Patient identifiers will not be part of the analytic database. Any paper subject records will be destroyed upon completion of analysis. Due to these precautions the likelihood of a loss of privacy or confidentially is very minimal.

All personnel involved with the DCC have signed confidentiality agreements concerning data encountered in the course of their daily work. All personnel (including administrative staff) have received Human Subjects Protection and Health Information Portability and Accountability Act (HIPAA) education. We require all users to sign specific agreements concerning security, confidentiality, and use of our information systems, before access is provided.

## 10.3 Potential Benefits

There is no immediate potential benefit to the human subjects involved in the study. There is future benefit to human subjects by improving the care of injured children through the knowledge that is gained by the study.

This study will develop and validate a pediatric CSI risk assessment tool that can be used by ED providers to determine which children can safely forgo spinal precautions and cervical spine imaging after blunt trauma. It will also lay the groundwork for determining the validity of this tool when used by other health care providers and for a subsequent implementation trial. A rigorously-tested risk assessment tool for CSI in children has the potential for substantially reducing the number of children who receive unnecessary spinal precautions for trauma transport and/or who receive radiographic clearance of their cervical spine. This could lead to significant changes in recommendations for the treatment and transport of injured children worldwide.

## 10.4 Waiver of Informed Consent

This study is a prospective observational study. We will be obtaining observations from clinicians regarding factors that place children at risk for CSI. To ensure that these observations are not biased, we must try to obtain the surveys before diagnostic imaging is performed. The decision to obtain diagnostic testing will not be influenced by enrollment in the study. Diagnostic testing for these children should not be delayed for study procedures. The proposed study meets all regulatory requirements for a waiver, as outlined in the Code of Federal Regulations Title 45 Part 46, "Protection of Human Subjects". Justification is provided below.

**45 C.F.R. 46.116 (d)(1) The research involves no more than minimal risk to the subjects** The research activities proposed in this application are 1) collection of observational data from ED and EMS personnel and 2) review of medical record data. Both of these are minimal risk activities.

**45 C.F.R. 46.116 (d)(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects** Beyond collection of observational data, there are no activities or interventions outside of routine clinical care. Nothing proposed in the research will adversely affect the rights and welfare of the subject.

**45 C.F.R. 46.116 (d)(3) The research could not practicably be carried out without the waiver or alteration** The research proposed in this application would

be impracticable to conduct if informed consent is required. This study investigates a rare disease, cervical spine injury (CSI). CSI occurs in less than 2% of children who sustain blunt trauma. We determined the feasibility of the proposed project's sample size 22,222 by using the enrollment rates and incidence of CSI in the pilot study and applying it to information regarding this study's participating sites obtained from PECARN's core data project.[92, 127]

Prior similar PECARN work in children with head injury and abdominal trauma has demonstrated that we are able to achieve enrollment rates of 80% only with waiver of consent.[96, 97] If written informed consent had been required for these prospective cohort participants, enrollment would have decreased by 45% due to lack of an available parent or legal guardian (LAR) during the emergency visit.[98, 99] Further, we have concern that the established cohort would not be representative of the spectrum of children at risk for CSI and thus would result in ascertainment bias. Our prior work has demonstrated that those patients at highest risk for severe injury will be more difficult to consent (e.g. absent guardian, time critical injuries, etc.) while lower risk patients will be easier to consent (e.g. arrive with guardian, stable injuries etc.).[98, 99] Additional considerations regarding the impact of written informed consent on the study's scientific integrity:

- Pivotal to the scientific integrity of developing a decision tool is that observational data collected from proxies is collected before diagnostic testing is obtained and/or reviewed. Observational data obtained after the ED provider is aware of testing results introduces recall bias. It would be unethical, however, to delay patient care in order to obtain written informed consent for collection of observational assessment data from EMS and ED providers. Thus, either we delay collection of observational assessment data for the written informed consent and risk the introduction of recall bias OR we conduct the collection of observational assessment data under waiver of consent.

- In trauma situations, parents may be under considerable duress given the critical nature of their child's injuries. While it is not uncommon for parents/patients to be approached for consent under these circumstances, particularly for studies and clinical procedures that may have substantial benefit to the patient, it would be inappropriate to solicit informed consent for a minimal risk study during this sensitive period of time when parents are facing more pressing decisions.

- Data are to be collected from EMS prehospital personnel, who are required to return to service within 30 minutes or sooner of hospital arrival. It is implausible that we would be able to obtain written informed consent from a parent or legal guardian prior to EMS departure from the ED. Thus, we would be unable to collect

prospective information from the EMS provider which threatens an important aim of the study.

- For missed eligible subjects, we will not know who is eligible until review of the ED daily census reports, at which juncture, the patient will no longer be in the ED making consent procedures impossible.

**45 C.F.R. 46.116 (d)(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation** Guardians of eligible children will be provided a Consent, Parental Permission, and Authorization cover letter from the enrolling physician or research coordinator regarding the study. This handout will be provided in the ED, if the legal guardian is present. If the child does not undergo cervical spine imaging in the ED, a follow-up call will be made to the legal guardian to confirm absence of CSI. At the time of the phone call, the Research Coordinator will confirm that the legal guardian has received the cover letter and obtain verbal consent for the phone follow-up questions.

## 10.5 Health Insurance Portability and Accountability Act

Data elements collected include the date of birth and date of admission. Prior to statistical analyses, dates will be used to calculate patient age at the time of the study events. The final data sets (used for study analyses and archived at the end of the study) will be de–identified, and will exclude these specific dates.

Data elements for race, ethnicity, and gender are also being collected. These demographic data are required for Federal reporting purposes to delineate subject accrual by race, ethnicity, and gender.

For purposes of the DCC handling potential protected health information (PHI) and producing the de–identified research data sets that will be used for analyses, all study sites have been offered a Business Associate Agreement with the University of Utah. Copies of executed Business Associate Agreements are maintained at the DCC.

## 10.6 Inclusion of Women and Minorities

The proposed subject criteria were selected to represent the population of children who may be at risk for CSI and in whom there are not clinical guidelines for evaluation and management. The gender, race and ethnicity of the study cohort will be demographically

representative of children who experience blunt trauma and who are cared for at the participating study sites. The PHS Inclusion Enrollment Report represents the expected demographic breakdown of the study population by gender, race and ethnicity. There will be no sex/gender, racial or ethnic group excluded for any reason. As such, no outreach programs are proposed for the purpose of recruiting specific sex/gender, racial, or ethnic group members.

## 10.7 ClinicalTrials.gov Requirements

This study will not be registered at ClinicalTrials.gov as it is not an interventional trial.

## 10.8 Retention of Records

For federally funded studies subject to the Common Rule, records relating to the research conducted shall be retained for at least 3 years after completion of the research. Completion of the research for this protocol should be anticipated to include planned primary and secondary analyses, as well as subsequent derivative analyses. Completion of the research also entails completion of all publications relating to the research. All records shall be accessible for inspection and copying by authorized representatives of the regulatory authorities at reasonable times and in a reasonable manner [45 CFR §46.115(b)].

## 10.9 Public Use Data Set

After subject enrollment and follow up have been completed, the DCC will prepare a final study dataset for analysis. A releasable database will be produced and completely de-identified in accordance with the definitions provided in the Health insurance Portability and Accountability Act (HIPAA). Namely, all identifiers specified in HIPAA will be recoded in a manner that will make it impossible to deduce or impute the specific identity of any patient. The database will not contain any institutional identifiers.

The DCC will also prepare a data dictionary that provides a concise definition of every data element included in the database. If specific data elements have idiosyncrasies that might affect interpretation or analysis, this will be discussed in the dictionary document. In accordance with policies determined by the investigators and funding sponsors, the releasable database will be provided to users in electronic form.

# References

[1] J. R. Leonard, D. M. Jaffe, N. Kuppermann, C. S. Olsen, J. C. Leonard, and Group Pediatric Emergency Care Applied Research Network Cervical Spine Study. Cervical spine injury patterns in children. *Pediatrics*, 133(5):e1179–88, 2014.

[2] P. Viccellio, H. Simon, B. D. Pressman, M. N. Shah, W. R. Mower, J. R. Hoffman, and Nexus Group. A prospective multicenter study of cervical spine injury in children. *Pediatrics*, 108(2):E20, 2001.

[3] *Advance Trauma Life Support for Doctors: Student Course Manual*. American College of Surgeons, Chicago, IL, ninth edition, 2012.

[4] I. Kwan, F. Bunn, and I. Roberts. Spinal immobilisation for trauma patients. *Cochrane Database Syst Rev*, (2):CD002803, 2001.

[5] M. Hauswald, G. Ong, D. Tandberg, and Z. Omar. Out-of-hospital spinal immobilization: its effect on neurologic injury. *Acad Emerg Med*, 5(3):214–9, 1998.

[6] G. L. Foltin, P. Dayan, M. Tunik, M. Marr, J. Leonard, K. Brown, Jr. Hoyle, J., E. B. Lerner, and Network Prehospital Working Group of the Pediatric Emergency Care Applied Research. Priorities for pediatric prehospital research. *Pediatr Emerg Care*, 26(10):773–7, 2010.

[7] J. E. Herzenberg, R. N. Hensinger, D. K. Dedrick, and W. A. Phillips. Emergency transport and positioning of young children who have an injury of the cervical spine. the standard backboard may be hazardous. *J Bone Joint Surg Am*, 71(1):15–22, 1989.

[8] M. Nypaver and D. Treloar. Neutral cervical spine positioning in children. *Ann Emerg Med*, 23(2):208–11, 1994.

[9] D. L. Schriger, B. Larmon, T. LeGassick, and T. Blinman. Spinal immobilization on a flat backboard: does it result in neutral position of the cervical spine? *Ann Emerg Med*, 20(8):878–81, 1991.

[10] R. A. De Lorenzo, J. E. Olson, M. Boska, R. Johnston, G. C. Hamilton, J. Augustine, and R. Barton. Optimal positioning for cervical immobilization. *Ann Emerg Med*, 28(3):301–8, 1996.

[11] C. Curran, A. M. Dietrich, M. J. Bowman, M. E. Ginn-Pease, D. R. King, and E. Kosnik. Pediatric cervical-spine immobilization: achieving neutral position? *J Trauma*, 39(4):729–32, 1995.

[12] E. B. Lerner, A. J. th Billittier, and R. M. Moscati. The effects of neutral positioning with and without padding on spinal immobilization of healthy subjects. *Prehosp Emerg Care*, 2(2):112–6, 1998.

[13] H. B. Boswell, A. Dietrich, W. E. Shiels, D. King, M. Ginn-Pease, M. J. Bowman, and W. H. Cotton. Accuracy of visual determination of neutral position of the immobilized pediatric cervical spine. *Pediatr Emerg Care*, 17(1):10–4, 2001.

[14] P. Ben-Galim, N. Dreiangel, K. L. Mattox, C. A. Reitman, S. B. Kalantar, and J. A. Hipp. Extrication collars can result in abnormal separation between vertebrae in the presence of a dissociative injury. *J Trauma*, 69(2):447–50, 2010.

[15] G. B. Bell. Spinal cord injury, pressure ulcers, and support surfaces. *Ostomy Wound Manage*, 45(6):48–50, 52–3, 1999.

[16] H. A. Linares, A. R. Mawson, E. Suarez, and J. J. Biundo. Association between pressure sores and immobilization in the immediate post-injury period. *Orthopedics*, 10(4):571–3, 1987.

[17] A. R. Mawson, Jr. Biundo, J. J., P. Neville, H. A. Linares, Y. Winchester, and A. Lopez. Risk factors for early occurring pressure ulcers following spinal cord injury. *Am J Phys Med Rehabil*, 67(3):123–7, 1988.

[18] F. Sheerin and R. de Frein. The occipital and sacral pressures experienced by healthy volunteers under spinal immobilization: a trial of three surfaces. *J Emerg Nurs*, 33(5):447–50, 2007.

[19] G. Davies, C. Deakin, and A. Wilson. The effect of a rigid collar on intracranial pressure. *Injury*, 27(9):647–9, 1996.

[20] J. B. Brown, P. E. Bankey, A. T. Sangosanya, J. D. Cheng, N. A. Stassen, and M. L. Gestring. Prehospital spinal immobilization does not appear to be beneficial and may complicate care following gunshot injury to the torso. *J Trauma*, 67(4):774–8, 2009.

[21] E. R. Haut, B. T. Kalish, D. T. Efron, A. H. Haider, K. A. Stevens, A. N. Kieninger, 3rd Cornwell, E. E., and D. C. Chang. Spine immobilization in penetrating trauma: more harm than good? *J Trauma*, 68(1):115–20; discussion 120–1, 2010.

[22] K. J. Heath. The effect of laryngoscopy of different cervical spine immobilisation techniques. *Anaesthesia*, 49(10):843–5, 1994.

[23] R. W. Schafermeyer, B. M. Ribbeck, J. Gaskins, S. Thomason, M. Harlan, and A. Attkisson. Respiratory effects of spinal immobilization in children. *Ann Emerg Med*, 20(9):1017–9, 1991.

[24] D. Bauer and R. Kowalski. Effect of spinal immobilization devices on pulmonary function in the healthy, nonsmoking man. *Ann Emerg Med*, 17(9):915–8, 1988.

[25] V. Y. Totten and D. B. Sugarman. Respiratory effects of spinal immobilization. *Prehosp Emerg Care*, 3(4):347–52, 1999.

[26] D. Chan, R. Goldberg, A. Tascone, S. Harmon, and L. Chan. The effect of spinal immobilization on healthy volunteers. *Ann Emerg Med*, 23(1):48–51, 1994.

[27] D. Chan, R. M. Goldberg, J. Mason, and L. Chan. Backboard versus mattress splint immobilization: a comparison of symptoms generated. *J Emerg Med*, 14(3):293–8, 1995.

[28] W. H. Cordell, J. C. Hollingsworth, M. L. Olinger, S. J. Stroman, and D. R. Nelson. Pain and tissue-interface pressures during spine-board immobilization. *Ann Emerg Med*, 26(1):31–6, 1995.

[29] D. A. Cross and J. Baskerville. Comparison of perceived pain with different immobilization techniques. *Prehosp Emerg Care*, 5(3):270–4, 2001.

[30] J. C. Leonard, J. Mao, and D. M. Jaffe. Potential adverse effects of spinal immobilization in children. *Prehosp Emerg Care*, 16(4):513–8, 2012.

[31] J. A. March, S. C. Ausband, and L. H. Brown. Changes in physical examination caused by use of spinal immobilization. *Prehosp Emerg Care*, 6(4):421–4, 2002.

[32] E. G. Kim, K. M. Brown, J. C. Leonard, D. M. Jaffe, C. S. Olsen, N. Kuppermann, and C. Spine Study Group of the Pediatric Emergency Care Applied Research Network. Variability of prehospital spinal immobilization in children at risk for cervical spine injury. *Pediatr Emerg Care*, 29(4):413–8, 2013.

[33] R. Mannix, L. E. Nigrovic, S. A. Schutzman, K. Hennelly, F. T. Bourgeois, W. P. Meehan, G. Fleisher, M. Monuteaux, and L. K. Lee. Factors associated with the use of cervical spine computed tomography imaging in pediatric trauma patients. *Acad Emerg Med*, 18(9):905–11, 2011.

[34] J. Broder, L. A. Fordham, and D. M. Warshauer. Increasing utilization of computed tomography in the pediatric emergency department, 2000-2006. *Emerg Radiol*, 14(4):227–32, 2007.

[35] K. M. Adelgais, D. C. Grossman, S. G. Langer, and F. A. Mann. Use of helical computed tomography for imaging the pediatric cervical spine. *Acad Emerg Med*, 11(3):228–36, 2004.

[36] P. J. Schenarts, J. Diaz, C. Kaiser, Y. Carrillo, V. Eddy, and Jr. Morris, J. A. Prospective comparison of admission computed tomographic scan and plain films of the upper cervical spine in trauma patients with altered mental status. *J Trauma*, 51(4):663–8; discussion 668–9, 2001.

[37] J. B. Frank, C. K. Lim, J. M. Flynn, and J. P. Dormans. The efficacy of magnetic resonance imaging in pediatric cervical spine clearance. *Spine (Phila Pa 1976)*, 27(11):1176–9, 2002.

[38] M. M. Griffen, E. R. Frykberg, A. J. Kerwin, M. A. Schinco, J. J. Tepas, K. Rowe, and J. Abboud. Radiographic clearance of blunt cervical spine injury: plain radiograph or computed tomography scan? *J Trauma*, 55(2):222–6; discussion 226–7, 2003.

[39] R. Smith-Bindman, D. L. Miglioretti, E. Johnson, C. Lee, H. S. Feigelson, M. Flynn, R. T. Greenlee, R. L. Kruger, M. C. Hornbrook, D. Roblin, L. I. Solberg, N. Vanneman, S. Weinmann, and A. E. Williams. Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. *JAMA*, 307(22):2400–9, 2012.

[40] R. A. Kleinerman. Cancer risks following diagnostic and therapeutic radiation exposure in children. *Pediatr Radiol*, 36 Suppl 2:121–5, 2006.

[41] Health risks from exposure to low levels of ionizing radiation: Beir vii phase 2. Report, 2006.

[42] E. J. Hall. Lessons we have learned from our children: cancer risks from diagnostic radiology. *Pediatr Radiol*, 32(10):700–6, 2002.

[43] M. S. Pearce, J. A. Salotti, M. P. Little, K. McHugh, C. Lee, K. P. Kim, N. L. Howe, C. M. Ronckers, P. Rajaraman, A. W. Sir Craft, L. Parker, and A. Berrington de Gonzalez. Radiation exposure from ct scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. *Lancet*, 380(9840):499–505, 2012.

[44] D. Brenner, C. Elliston, E. Hall, and W. Berdon. Estimated risks of radiation-induced fatal cancer from pediatric ct. *AJR Am J Roentgenol*, 176(2):289–96, 2001.

[45] D. J. Brenner. Estimating cancer risks from pediatric ct: going from the qualitative to the quantitative. *Pediatr Radiol*, 32(4):228–1; discussion 242–4, 2002.

[46] P. N. Chan, G. E. Antonio, J. F. Griffith, K. W. Yu, T. H. Rainer, and A. T. Ahuja. Computed tomography for cervical spine trauma. the impact of mdct on fracture detection and dose deposition. *Emerg Radiol*, 11(5):286–90, 2005.

[47] R. R. Jimenez, M. A. Deguzman, S. Shiran, A. Karrellas, and R. L. Lorenzo. Ct versus plain radiographs for evaluation of c-spine injury in young children: do benefits outweigh risks? *Pediatr Radiol*, 38(6):635–44, 2008.

[48] A. Berrington de Gonzalez, M. Mahesh, K. P. Kim, M. Bhargavan, R. Lewis, F. Mettler, and C. Land. Projected cancer risks from computed tomographic scans performed in the united states in 2007. *Arch Intern Med*, 169(22):2071–7, 2009.

[49] K. Faulkner and B. M. Moores. Radiation dose and somatic risk from computed tomography. *Acta Radiol*, 28(4):483–8, 1987.

[50] R. D. Muchow, K. R. Egan, W. W. Peppler, and P. A. Anderson. Theoretical increase of thyroid cancer induction from cervical spine multidetector computed tomography in pediatric trauma patients. *J Trauma Acute Care Surg*, 72(2):403–9, 2012.

[51] M. J. Adams, R. E. Shore, A. Dozier, S. E. Lipshultz, R. G. Schwartz, L. S. Constine, T. A. Pearson, M. Stovall, K. Thevenet-Morrison, and S. G. Fisher. Thyroid cancer risk 40+ years after irradiation for an enlarged thymus: an update of the hempelmann cohort. *Radiat Res*, 174(6):753–62, 2010.

[52] P. Bhatti, L. H. Veiga, C. M. Ronckers, A. J. Sigurdson, M. Stovall, S. A. Smith, R. Weathers, W. Leisenring, A. C. Mertens, S. Hammond, D. L. Friedman, J. P. Neglia, A. T. Meadows, S. S. Donaldson, C. A. Sklar, L. L. Robison, and P. D. Inskip. Risk of second primary thyroid cancer after radiotherapy for a childhood cancer in a large cohort study: an update from the childhood cancer survivor study. *Radiat Res*, 174(6):741–52, 2010.

[53] Risk to the thyroid from ionizing radiation. Report NCRP Report No. 159, National Council on Radiation Protection and Measurements, 2008.

[54] E. Ron, J. H. Lubin, R. E. Shore, K. Mabuchi, B. Modan, L. M. Pottern, A. B. Schneider, M. A. Tucker, and Jr. Boice, J. D. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. *Radiat Res*, 141(3):259–77, 1995.

[55] A. B. Schneider, E. Ron, J. Lubin, M. Stovall, and T. C. Gierlowski. Dose-response relationships for radiation-induced thyroid cancer and thyroid nodules: evidence for the prolonged effects of radiation on the thyroid. *J Clin Endocrinol Metab*, 77(2):362–9, 1993.

[56] John D. Mathews, Anna V. Forsythe, Zoe Brady, Martin W. Butler, Stacy K. Goergen, Graham B. Byrnes, Graham G. Giles, Anthony B. Wallace, Philip R. Anderson, Tenniel A. Guiver, Paul McGale, Timothy M. Cain, James G. Dowty, Adrian C. Bickerstaffe, and Sarah C. Darby. Cancer risk in 680?000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million australians. *The BMJ*, 346:f2360, 2013.

[57] H. K. Koh, J. J. Piotrowski, S. Kumanyika, and J. E. Fielding. Healthy people: a 2020 vision for the social determinants approach. *Health Educ Behav*, 38(6):551–7, 2011.

[58] Cdc injury research agenda, 2009-2018. Report, National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, US Department of Health and Human Services, 2009.

[59] M. R. Sayre, L. J. White, L. H. Brown, S. D. McHenry, and E. M. S. Research Strategic Plan Writing Team National. The national ems research strategic plan. *Prehosp Emerg Care*, 9(3):255–66, 2005.

[60] M. R. Sayre, L. J. White, L. H. Brown, S. D. McHenry, and Participants Implementation Symposium. National ems research agenda: proceedings of the implementation symposium. *Acad Emerg Med*, 10(10):1100–8, 2003.

[61] J. S. Seidel, D. Henderson, S. Tittle, D. Jaffe, D. Spaite, J. M. Dean, M. Gausche, R. J. Lewis, A. Cooper, A. Zaritsky, T. Espisito, and D. Maederis. Priorities for research in emergency medical services for children: results of a consensus conference. *Pediatr Emerg Care*, 15(1):55–8, 1999.

[62] Emergency medical services for children. Report, Institute of Medicine, 1993.

[63] Emergency care for children: Growing pains. Report, Institute of Medicine, 2007.

[64] Emergency medical services: At the crossroads. Report, Institute of Medicine, 2007.

[65] D. C. Cone. Knowledge translation in the emergency medical services: a research agenda for advancing prehospital care. *Acad Emerg Med*, 14(11):1052–7, 2007.

[66] R. F. Maio, H. G. Garrison, D. W. Spaite, J. S. Desmond, M. A. Gregor, C. G. Cayten, Jr. Chew, J. L., E. M. Hill, S. M. Joyce, E. J. MacKenzie, D. R. Miller, P. J. O'Malley, and I. G. Stiell. Emergency medical services outcomes project i (emsop i): prioritizing conditions for outcomes research. *Ann Emerg Med*, 33(4):423–32, 1999.

[67] S. Z. Miller, H. Rincon, N. Kuppermann, and Network Pediatric Emergency Care Applied Research. Revisiting the emergency medicine services for children research agenda: priorities for multicenter research in pediatric emergency care. *Acad Emerg Med*, 15(4):377–83, 2008.

[68] Gap analysis of ems related research: Report to the federal interagency committee on ems. Report, EMSC National Resource Center, 2009.

[69] J. R. Hoffman, D. L. Schriger, W. Mower, J. S. Luo, and M. Zucker. Low-risk criteria for cervical-spine radiography in blunt trauma: a prospective study. *Ann Emerg Med*, 21(12):1454–60, 1992.

[70] J. R. Hoffman, W. R. Mower, A. B. Wolfson, K. H. Todd, and M. I. Zucker. Validity of a set of clinical criteria to rule out injury to the cervical spine in patients with blunt trauma. national emergency x-radiography utilization study group. *N Engl J Med*, 343(2):94–9, 2000.

[71] S. Mahadevan, W. R. Mower, J. R. Hoffman, N. Peeples, W. Goldberg, and R. Sonner. Interrater reliability of cervical spine injury criteria in patients with blunt trauma. *Ann Emerg Med*, 31(2):197–201, 1998.

[72] M. Touger, P. Gennis, N. Nathanson, D. W. Lowery, Jr. Pollack, C. V., J. R. Hoffman, and W. R. Mower. Validity of a decision rule to reduce cervical spine radiography in elderly patients with blunt trauma. *Ann Emerg Med*, 40(3):287–93, 2002.

[73] I. G. Stiell, G. A. Wells, K. L. Vandemheen, C. M. Clement, H. Lesiuk, V. J. De Maio, A. Laupacis, M. Schull, R. D. McKnight, R. Verbeek, R. Brison, D. Cass, J. Dreyer, M. A. Eisenhauer, G. H. Greenberg, I. MacPhail, L. Morrison, M. Reardon, and J. Worthington. The canadian c-spine rule for radiography in alert and stable trauma patients. *JAMA*, 286(15):1841–8, 2001.

[74] I. G. Stiell, C. M. Clement, R. D. McKnight, R. Brison, M. J. Schull, B. H. Rowe, J. R. Worthington, M. A. Eisenhauer, D. Cass, G. Greenberg, I. MacPhail, J. Dreyer, J. S. Lee, G. Bandiera, M. Reardon, B. Holroyd, H. Lesiuk, and G. A. Wells. The canadian c-spine rule versus the nexus low-risk criteria in patients with trauma. *N Engl J Med*, 349(26):2510–8, 2003.

[75] D. Kerr, L. Bradshaw, and A. M. Kelly. Implementation of the canadian c-spine rule reduces cervical spine x-ray rate for alert patients with potential neck injury. *J Emerg Med*, 28(2):127–31, 2005.

[76] I. G. Stiell, C. M. Clement, J. Grimshaw, R. J. Brison, B. H. Rowe, M. J. Schull, J. S. Lee, J. Brehaut, R. D. McKnight, M. A. Eisenhauer, J. Dreyer, E. Letovsky, T. Rutledge, I. MacPhail, S. Ross, A. Shah, J. J. Perry, B. R. Holroyd, U. Ip, H. Lesiuk, and G. A. Wells. Implementation of the canadian c-spine rule: prospective 12 centre cluster randomised trial. *BMJ*, 339:b4146, 2009.

[77] D. Muhr, D. L. Seabrook, and L. K. Wittwer. Paramedic use of a spinal injury clearance algorithm reduces spinal immobilization in the out-of-hospital setting. *Prehosp Emerg Care*, 3(1):1–6, 1999.

[78] G. Stroh and D. Braude. Can an out-of-hospital cervical spine clearance protocol identify all patients with injuries? an argument for selective immobilization. *Ann Emerg Med*, 37(6):609–15, 2001.

[79] R. M. Domeier, R. A. Swor, R. W. Evans, J. B. Hancock, W. Fales, J. Krohmer, S. M. Frederiksen, E. J. Rivera-Rivera, and M. A. Schork. Multicenter prospective validation of prehospital clinical spinal clearance criteria. *J Trauma*, 53(4):744–50, 2002.

[80] R. Sahni, J. J. Menegazzi, and Jr. Mosesso, V. N. Paramedic evaluation of clinical indicators of cervical spinal injury. *Prehosp Emerg Care*, 1(1):16–8, 1997.

[81] L. H. Brown, J. E. Gough, and W. B. Simonds. Can ems providers adequately assess trauma patients for cervical spinal injury? *Prehosp Emerg Care*, 2(1):33–36, 1998.

[82] S. W. Meldon, T. A. Brant, R. K. Cydulka, T. E. Collins, and B. R. Shade. Out-of-hospital cervical spine clearance: agreement between emergency medical technicians and emergency physicians. *J Trauma*, 45(6):1058–61, 1998.

[83] B. P. Armstrong, H. K. Simpson, R. Crouch, and C. D. Deakin. Prehospital clearance of the cervical spine: does it need to be a pain in the neck? *Emerg Med J*, 24(7):501–3, 2007.

[84] D. W. Spaite, E. A. Criss, T. D. Valenzuela, and J. Guisto. Emergency medical service systems research: problems of the past, challenges of the future. *Ann Emerg Med*, 26(2):146–52, 1995.

[85] M. Callaham. Quantifying the scanty science of prehospital emergency care. *Ann Emerg Med*, 30(6):785–90, 1997.

[86] J. C. Leonard, D. P. Scharff, V. Koors, E. B. Lerner, K. M. Adelgais, J. Anders, K. Brown, L. Babcock, R. Lichenstein, K. A. Lillis, and D. M. Jaffe. A qualitative assessment of factors that influence emergency medical services partnerships in prehospital research. *Acad Emerg Med*, 19(2):161–73, 2012.

[87] I. Rachesky, W. T. Boyce, B. Duncan, J. Bjelland, and B. Sibley. Clinical prediction of cervical spine injuries in children. radiographic abnormalities. *Am J Dis Child*, 141(2):199–201, 1987.

[88] D. M. Jaffe, H. Binns, M. A. Radkowski, M. J. Barthel, and 3rd Engelhard, H. H. Developing a clinical algorithm for early management of cervical spine injury in child trauma victims. *Ann Emerg Med*, 16(3):270–6, 1987.

[89] H. Binns, D. M. Jaffe, M. A. Radkowski, M. J. Barthel, and 3rd Engelhard, H. H. An eight-variable clinical assessment model for the prediction of cervical spine injury in children. *Am J Dis Child*, 141(12):1249–50, 1987.

[90] J. C. Leonard, N. Kuppermann, C. Olsen, L. Babcock-Cimpello, K. Brown, P. Mahajan, K. M. Adelgais, J. Anders, D. Borgialli, A. Donoghue, Jr. Hoyle, J. D., E. Kim, J. R. Leonard, K. A. Lillis, L. E. Nigrovic, E. C. Powell, G. Rebella, S. D. Reeves, A. J. Rogers, C. Stankovic, G. Teshome, D. M. Jaffe, and Network Pediatric Emergency Care Applied Research. Factors associated with cervical spine injury in children after blunt trauma. *Ann Emerg Med*, 58(2):145–55, 2011.

[91] J. C. Leonard, D. M. Jaffe, C. S. Olsen, and N. Kuppermann. Age-related differences in factors associated with cervical spine injuries in children. *Acad Emerg Med*, 22(4):441–6, 2015.

[92] F. A. Ahmad, H. Schwartz, L. R. Browne, S. Lassa-Claxton, M. Wallendorf, E. B. Lerner, N. Kuppermann, and J. C. Leonard. Methods for collecting paired observations from emergency medical services and emergency department providers for pediatric cervical spine injury risk factors. *Acad Emerg Med*, 2016.

[93] P. A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, and J. G. Conde. Research electronic data capture (redcap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*, 42(2):377–81, 2009.

[94] JC Leonard, LB Browne, H Schwartz, FA Ahmad, MJ Wallendorf, EB Lerner, and N Kuppermann. Prospective evaluation of the pediatric emergency care applied research network (pecarn) cervical spine injury risk factors. In *Pediatric Academic Societies*.

[95] J. C. Leonard. Cervical spine injury. *Pediatr Clin North Am*, 60(5):1123–37, 2013.

[96] J. F. Holmes, K. Lillis, D. Monroe, D. Borgialli, B. T. Kerrey, P. Mahajan, K. Adelgais, A. M. Ellison, K. Yen, S. Atabaki, J. Menaker, B. Bonsu, K. S. Quayle, M. Garcia, A. Rogers, S. Blumberg, L. Lee, M. Tunik, J. Kooistra, M. Kwok, L. J. Cook, J. M. Dean, P. E. Sokolove, D. H. Wisner, P. Ehrlich, A. Cooper, P. S. Dayan, S. Wootton-Gorges, N. Kuppermann, and Network Pediatric Emergency Care Applied Research. Identifying children at very low risk of clinically important blunt abdominal injuries. *Ann Emerg Med*, 62(2):107–116 e2, 2013.

[97] N. Kuppermann, J. F. Holmes, P. S. Dayan, Jr. Hoyle, J. D., S. M. Atabaki, R. Holubkov, F. M. Nadel, D. Monroe, R. M. Stanley, D. A. Borgialli, M. K. Badawy, J. E. Schunk, K. S. Quayle, P. Mahajan, R. Lichenstein, K. A. Lillis, M. G. Tunik, E. S. Jacobs, J. M. Callahan, M. H. Gorelick, T. F. Glass, L. K. Lee, M. C. Bachman, A. Cooper, E. C. Powell, M. J. Gerardi, K. A. Melville, J. P. Muizelaar, D. H. Wisner, S. J. Zuspan, J. M. Dean, S. L. Wootton-Gorges, and Network Pediatric Emergency Care Applied Research. Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. *Lancet*, 374(9696):1160–70, 2009.

[98] J. F. Holmes, R. Holubkov, N. Kuppermann, and Network Pediatric Emergency Care Applied Research. Guardian availability in children evaluated in the emergency department for blunt head trauma. *Acad Emerg Med*, 16(1):15–20, 2009.

[99] R. M. Stanley, M. D. Johnson, C. Vance, L. Bajaj, L. Babcock, S. Atabaki, D. Thomas, H. K. Simon, D. M. Cohen, D. Rubacalva, P. David Adelson, B. Bulloch,

A. J. Rogers, P. Mahajan, J. Baren, L. Lee, J. Hoyle, K. Quayle, T. Charles Casper, J. Michael Dean, N. Kuppermann, and Network Pediatric Emergency Care Applied Research. Challenges enrolling children into traumatic brain injury trials: An observational study. *Acad Emerg Med*, 24(1):31–39, 2017.

[100] H Browne, LR Schwartz, FA Ahmad, M Wallendorf, N Kuppermann, EB Lerner, and JC Leonard. Inter-observer agreement in pediatric cervical spine injury (csi) risk assessment between emergency medical services (ems) and emergency department (ed) providers. In *Pediatric Academic Societies*.

[101] A. F. Sullivan, S. A. Rudders, A. L. Gonsalves, A. P. Steptoe, J. A. Espinola, and Jr. Camargo, C. A. National survey of pediatric services available in us emergency departments. *Int J Emerg Med*, 6(1):13, 2013.

[102] J. Athey, J. M. Dean, J. Ball, R. Wiebe, and I. Melese-d'Hospital. Ability of hospitals to care for pediatric emergency patients. *Pediatr Emerg Care*, 17(3):170–4, 2001.

[103] J Neilson. The usability engineering life cycle. *Computer*, 25(3):12–22, 1992.

[104] D. J. Mayhew. *The usability engineering lifecycle*, pages 147–148. ACM, 1999.

[105] L. G. Militello and R. J. Hutton. Applied cognitive task analysis (acta): a practitioner's toolkit for understanding cognitive task demands. *Ergonomics*, 41(11):1618–41, 1998.

[106] F. W. Taylor. *The Principles of Scientic Management*. Harper, New Yorker, 1911.

[107] N. A. Stanton. Hierarchical task analysis: developments, applications, and extensions. *Appl Ergon*, 37(1):55–79, 2006.

[108] A. D. Levi, R. J. Hurlbert, P. Anderson, M. Fehlings, R. Rampersaud, E. M. Massicotte, J. C. France, J. C. Le Huec, R. Hedlund, and P. Arnold. Neurologic deterioration secondary to unrecognized spinal instability following trauma–a multicenter study. *Spine (Phila Pa 1976)*, 31(4):451–8, 2006.

[109] Gregory P. Lekovic and Timothy R. Harrington. Litigation of missed cervical spine injuries in patients presenting with blunt traumatic injury. *Neurosurgery*, 60(3):516–523, 2007.

[110] Centers for Disease Control and Prevention (CDC). Vital signs: Unintentional injury deaths among persons aged 0-19 years - united states, 2000-2009. *MMWR. Morbidity and mortality weekly report*, 61:270–276, April 2012.

[111] Bayram Cirak, Suzan Ziegfeld, Vinita Misra Knight, David Chang, Anthony M. Avellino, and Charles N. Paidas. Spinal injuries in children. *Journal of pediatric surgery*, 39:607–612, April 2004.

[112] B. J. McGrory, R. A. Klassen, E. Y. Chao, J. W. Staeheli, and A. L. Weaver. Acute fractures and dislocations of the cervical spine in children and adolescents. *The Journal of bone and joint surgery. American volume*, 75:988–995, July 1993.

[113] Brian R. Englum, Cassandra Villegas, Oluwaseyi Bolorunduro, Elliott R. Haut, Edward E. Cornwell, David T. Efron, and Adil H. Haider. Racial, ethnic, and insurance status disparities in use of posthospitalization care after trauma. *Journal of the American College of Surgeons*, 213:699–708, December 2011.

[114] Shelby Chun Fat, Juan P. Herrera-Escobar, Anupamaa J. Seshadri, Syeda S. Al Rafai, Zain G. Hashmi, Elzerie de Jager, Constantine Velmahos, George Kasotakis, George Velmahos, Ali Salim, Adil H. Haider, and Deepika Nehra. Racial disparities in post-discharge healthcare utilization after trauma. *American journal of surgery*, 218:842–846, November 2019.

[115] Adil H. Haider, Paul Logan Weygandt, Jessica M. Bentley, Maria Francesca Monn, Karim Abdur Rehman, Benjamin L. Zarzaur, Marie L. Crandall, Edward E. Cornwell, and Lisa A. Cooper. Disparities in trauma care and outcomes in the united states: a systematic review and meta-analysis. *The journal of trauma and acute care surgery*, 74:1195–1205, May 2013.

[116] William H. Leukhardt, Joseph F. Golob, Andy M. McCoy, Adam M. A. Fadlalla, Mark A. Malangoni, and Jeffrey A. Claridge. Follow-up disparities after trauma: a real problem for outcomes research. *American journal of surgery*, 199:348–52; discussion 353, March 2010.

[117] Kevin Fiscella and David R. Williams. Health disparities based on socioeconomic inequities: implications for urban health care. *Academic medicine : journal of the Association of American Medical Colleges*, 79:1139–1147, December 2004.

[118] J Neilson. *Usability inspection methods*, pages 413–4. ACM, 1994.

[119] Bias R. G. Bailey R. Molich R. Dumas J. & Spool J. M Redish, J. G. *Usability in practice: formative usability evaluations-evolution and revolution*, pages 885–890. 2002.

[120] D. Sy. Adapting usability investigations for agile user-centered design. *Journal of computing systems*, 2(3):112–32, 2007.

[121] E. G. Poon, S. J. Wang, T. K. Gandhi, D. W. Bates, and G. J. Kuperman. Design and implementation of a comprehensive outpatient results manager. *J Biomed Inform*, 36(1-2):80–91, 2003.

[122] A. F. Rose, J. L. Schnipper, E. R. Park, E. G. Poon, Q. Li, and B. Middleton. Using qualitative studies to improve the usability of an emr. *J Biomed Inform*, 38(1):51–60, 2005.

[123] E. Tham, M. Swietlik, S. Deakyne, J. M. Hoffman, R. W. Grundmeier, M. D. Paterno, B. H. Rocha, M. H. Schaeffer, D. Pabbathi, E. Alessandrini, D. Ballard, H. S. Goldberg, N. Kuppermann, P. S. Dayan, and Pediat Emergency Care Appl Res Net. Clinical decision support for a multicenter trial of pediatric head trauma development, implementation, and lessons learned. *Applied Clinical Informatics*, 7(2):534–542, 2016.

[124] A. G. Fiks, S. L. Mayne, D. J. Karavite, A. Suh, R. O'Hara, A. R. Localio, M. Ross, and R. W. Grundmeier. Parent-reported outcomes of a shared decision-making portal in asthma: a practice-based rct. *Pediatrics*, 135(4):e965–73, 2015.

[125] A. G. Fiks, S. Mayne, D. J. Karavite, E. DeBartolo, and R. W. Grundmeier. A shared e-decision support portal for pediatric asthma. *J Ambul Care Manage*, 37(2):120–6, 2014.

[126] A. G. Fiks, P. Zhang, A. R. Localio, S. Khan, R. W. Grundmeier, D. J. Karavite, C. Bailey, E. A. Alessandrini, and C. B. Forrest. Adoption of electronic medical record-based decision support for otitis media in children. *Health Serv Res*, 50(2):489–513, 2015.

[127] E. R. Alpern, R. M. Stanley, M. H. Gorelick, A. Donaldson, S. Knight, S. J. Teach, T. Singh, P. Mahajan, J. G. Goepp, N. Kuppermann, J. M. Dean, J. M. Chamberlain, and Network Pediatric Emergency Care Applied Research. Epidemiology of a pediatric emergency medicine research network: the pecarn core data project. *Pediatr Emerg Care*, 22(10):689–99, 2006.