The Canadian CT Head Rule Study for Patients With Minor Head Injury: Rationale, Objectives, and Methodology for Phase I (Derivation)

Head injuries are among the most common types of trauma seen in North American emergency departments, with an estimated 1 million cases seen annually.1 Some of these patients die or suffer serious morbidity requiring months of hospitalization and rehabilitation. Many others, however, are classified as having a “minimal” or “minor” head injury (sometimes known as “mild”) is defined by a history of loss of consciousness, amnesia, or disorientation in a patient who is conscious and talking, that is, with a Glasgow Coma Scale score of 13 to 15. Although most patients with minor head injury can be discharged without sequelae after a period of observation, in a small proportion, their neurologic condition deteriorates and requires neurosurgical intervention for intracranial hematoma. The objective of the Canadian CT Head Rule Study is to develop an accurate and reliable decision rule for the use of computed tomography (CT) in patients with minor head injury. Such a decision rule would allow physicians to be more selective in their use of CT without compromising care of patients with minor head injury. This paper describes in detail the rationale, objectives, and methodology for Phase I of the study in which the decision rule was derived.

Head injuries are among the most common types of trauma seen in North American emergency departments, with an estimated 1 million cases seen annually.1 Some of these patients die or suffer serious morbidity requiring months of hospitalization and rehabilitation. Many others, however, are classified as having a “minimal” or “minor” head injury (sometimes known as “mild”) is defined by a history of loss of consciousness, amnesia, or disorientation in a patient who is conscious and talking, that is, with a Glasgow Coma Scale score of 13 to 15. Although most patients with minor head injury can be discharged without sequelae after a period of observation, in a small proportion, their neurologic condition deteriorates and requires neurosurgical intervention for intracranial hematoma. The objective of the Canadian CT Head Rule Study is to develop an accurate and reliable decision rule for the use of computed tomography (CT) in patients with minor head injury. Such a decision rule would allow physicians to be more selective in their use of CT without compromising care of patients with minor head injury. This paper describes in detail the rationale, objectives, and methodology for Phase I of the study in which the decision rule was derived.

injury. Patients with “minimal” head injury have not experienced loss of consciousness or amnesia and rarely require admission to hospital. “Minor” head injury (sometimes known as “mild”) is defined by a history of loss of consciousness, amnesia, or disorientation in a patient who is conscious and talking (ie, with a Glasgow Coma Scale [GCS] score of 13 to 15. A typical review of head injury patients admitted to a neurosurgical service found that 5% of cases were “severe” (GCS score <8), 11% were “moderate” (GCS score 8 to 12), and 84% were “minor” (GCS score 13 to 15). 4

Although most patients with minor head injury can be discharged without sequelae after a period of observation, in a small proportion of patients, their neurologic condition deteriorates and requires neurosurgical intervention for intracranial hematoma. Neurosurgeons and emergency physicians alike are well aware of the phenomenon of patients who “talk and deteriorate” and that the key to saving these patients is early diagnosis of intracranial hematoma followed by early surgery. During the 1970s, it became apparent that excess mortality and delayed diagnosis could be reduced in head injury by early use of computed tomography (CT). At the same time, plain skull radiography has been discouraged because of its low yield in minor head injury and because of the greater utility of CT in moderate and severe head injury.10

In recent years, the use of CT for minor head injury has become increasingly common, particularly in North America. In 1992, an estimated 270,000 CT scans of the head were performed in US EDs for head injury. Typical US hospital charges for unenhanced CT range from US$500 to US$800, suggesting a national total cost of US$135 million to US$216 million. The US yield of CT for intracranial lesions in minor head injury has been estimated to be from 0.7% to 3.7%. Conversely, 96.3% to 99.3% of CT scans performed in the United States for patients with minor head injury would be expected to be normal and therefore not alter management. More selective use of this expensive high-technology investigation for patients with minor head injury could lead to significant reductions in North American health care costs.

There is, however, considerable disagreement in the literature as to the indications for CT in the large number of head trauma cases classified as “minor.” In North America, opinions are divided into 3 groups. The first, composed primarily of neurosurgeons, believe that CT scanning is indicated for all patients with minor head injury. Stein and Ross, who are both US neurosurgeons, have recently written, “We recommend routine and immediate cranial CT scanning of all head injury patients who have lost consciousness or are amnestic, even if all other physical findings are normal.” The American College of Surgeons teaches that, “Except for patients with trivial head injuries, all head-injured patients require CT scanning at some time.” The second group, composed of neurosurgeons, emergency physicians, and radiologists, recommend a very selective approach to use of CT scanning in minor head injury. This group also points out that even a normal CT scan in the ED does not preclude the later development of intracranial hematoma. Taheri, a neurosurgeon from Louisiana, et al write: “…safe discharge without universal computed tomographic evaluation or admission is possible and cost-efficient.” The third group offers no clear or unambiguous recommendations for use of CT scanning in minor head injury cases and often suggest that more studies are required.

European authors describe a very selective approach to CT scanning for minor head injury cases. In Italy, CT is only recommended if a fracture has been demonstrated on skull radiography. In Denmark, CT is rarely ordered and then only by a neurosurgeon. In the United Kingdom and Spain, CT is only recommended for cases with documented skull fracture, focal neurologic deficit, or deterioration in mental status.

Without the support of widely accepted guidelines, North American emergency physicians are likely to follow the conservative approach of ordering CT scans for most patients with minor head injury seen in EDs. This approach, previously described for ankle and knee injury patients, is fostered by the nature of ED practice: high case volumes, brief physician-patient contact, uncertain follow-up, and fear of medicolegal repercussions. There is a clear need for valid and reliable guidelines to allow physicians to be more selective in their use of CT without compromising care of patients with minor head injury.

**METHODOLOGIC STANDARDS FOR DECISION RULES**

Clinical decision (or prediction) rules attempt to reduce the uncertainty of medical decisionmaking by standardizing the collection and interpretation of clinical data. A decision rule is derived from original research and may be defined as a decision-making tool that incorporates 3 or more variables from the history, physical examination, or...
simple tests. These decision rules help clinicians with diagnostic or therapeutic decisions at the bedside. Recently, there has been an interest in the methodologic standards for their development; these are summarized in Figure 1. 57-60

A number of studies have been conducted in the past 10 years by neurosurgeons,3,9,13-16,19,21,23,24,26-28,33-40,44,46-49,61-63 and radiologists11,31 to identify high-risk findings that would clearly indicate which group of patients with minor head injury should have CT. Unfortunately, these studies suffer from great variability in design and none could be considered methodologically robust according to the criteria described in Figure 1. Some of these deficiencies are described in the following text.

The specific outcome measure varies considerably among the studies with some focusing on the findings of CT,3,16,19,23,26,27,29-31,33-35,40,41,61,62,64-65 some on whether or not neurosurgical intervention was required,3,13,28,44,63,66,67 and others on death or disability.11,48,49 In several studies, the outcome measure was not clear,14,39,46,47 and in most studies, assessment of outcome was not made in a blinded fashion. Among those studies that use CT as the primary outcome, some excluded basal or linear skull fractures as significant findings.3,41 The predictors assessed in various studies are described in detail in Figure 2. Although data were collected prospectively in about half of the studies,11,13,23,24,28,30,34,39,41,64-67 in very few were the predictor variables clearly standardized or documented on a data collection sheet. No study explicitly collected the predictor variables without knowledge of the outcome.

Figure 1.
Methodologic standards for the derivation of clinical decision rules.

1. The outcome or diagnosis to be predicted must be clearly defined and assessment should be made in a blinded fashion.
2. The clinical findings to be used as predictors must be clearly defined and standardized and their assessment must be done without knowledge of the outcome.
3. The reliability or reproducibility of the predictor findings must be demonstrated.
4. The subjects in the study should be selected without bias and should represent a wide spectrum of characteristics to increase generalizability.
5. The mathematical techniques for deriving the rules must be identified.
6. Decision rules should be clinically sensible: have a clear purpose, be relevant, demonstrate content validity, be concise, and be easy to use in the intended clinical application.
7. The accuracy of the decision rule in classifying patients with (sensitivity) and without (specificity) the targeted outcome should be demonstrated.

Furthermore, no study attempted to assess the reliability of the predictor variables by measurement of interobserver agreement.

The definition of subjects in previous studies has been very variable, making it difficult for physicians to interpret and apply the findings to their own patients. Minor head injury was defined as loss of consciousness or amnesia in many studies,3,13,15,16,19,21,23,24,28,35,40,44,61-63,66,67 not specified in many others.11,14,26,27,29-31,33,34,39,41,46-49,64,65 Patients were included with unspecified GCS scores in some studies,11,15,30,31,33,34,39,46,47,49,65 and in others were included with GCS scores of 15,14,16,40,48,61,64,67 14 or 15,23,24,27,44,66 or 13 to 15,3,13,19,21,26,28,35,41,62,63. Only 9 studies specified that subjects should be adults but used different age criteria: 18 years or older,27,40 16 years or older,28,35,41 and 14 years or older.14,33,44,62 Approximately half of the studies only considered patients who had been admitted to the hospital.9,13,15,16,19,21,23,24,27,28,33,44,46,48,49,62,63 Very few studies specified whether patients should be excluded on the basis of penetrating injury,24,29-31,35,39,40,41 presence of skull fracture,16,27,44 (time since the injury,19,30,40,64,66,67) timing of the GCS examination,13,19,21,23,24,48 presence of neurologic deficit,15,19,21,24,27,38 ethanol intoxication (no studies), associated injuries,3,24 transfer from another hospital,28,40 or pregnancy (no studies). Many studies had small sample sizes with fewer than 500 patients with minor head injury.15,16,23,24,26-30,39,41,44,48,49,64,66

The mathematical techniques were described in only some studies3,11,14,20-31,33-35,41,46,62-66 and were generally rudimentary; very few included multivariate analyses. Very few studies concluded with clear, simple guidelines that could be described as clinically sensible. Some studies attempted to determine the accuracy of their recommendations by calculating sensitivity and specificity.3,11,14,15,19,23,24,27,31,34,35,39,44,46,48 Few offered recommendations that were highly sensitive.

Only 5 studies made any attempt to prospectively validate guidelines.11,16,34,39,68 In 3 of these, the guidelines had been empirically developed by consensus rather than by primary data collection.11,16,38 One other study prospectively evaluated derived guidelines in a small sample of 273 patients.34 A recent article by Haydel et al68 has received prominent attention, but the proposed guidelines may not be sufficiently reliable, sensitive, or specific to safely and efficiently guide clinicians in their use of CT. Although the predictor variables in phase I of this study were well standardized, no assessment of their interobserver agreement was made and some potentially
Preparation, rationale, and goals for the Canadian CT Head and C-Spine Study

In 1994, the investigators conducted a workshop that convened experts in emergency medicine, neurosurgery, research methodology, and research coordination to discuss methodologic issues for the CT Head Rule project.

In 1995, the investigators conducted a pilot study that reviewed data from the EDs of 7 Canadian hospitals for a 12-month period. We determined (1) the number of eligible patients with minor head injury (N=1,702), (2) the prevalence of acute brain injury (6.2%), (3) the prevalence of epidural hematoma (0.5%), (4) the discharge rate from the ED (71.4%), (5) the referral fraction for CT (30.7%), and (6) the rate of CT scans with negative findings (79.9%). There was very large variation in use of CT among similar sites (from a low of 16.2% to a high of 70.4%) and among certified attending physicians (from 7% to 80%). Five cases of intracranial hematoma were “missed” in patients who did not have a CT scan on their first ED visit.

The investigators also conducted 2 mail surveys of the attitudes of emergency physicians toward decision rules. In late 1995, we surveyed 300 members of the Canadian Association of Emergency Physicians with an 81% response rate. Only 14.9% stated that they agree with recommendations that all minor head injury patients should undergo CT. Overall, 97.2% physicians indicated they would consider using a sensitive and reliable clinical decision rule for the use of CT for patients with minor head injury. Not surprisingly, the physicians would require a higher sensitivity for a rule to predict need for neurologic intervention (median 100%) than for a rule to identify any acute brain injury on CT (median 96%). In 1998, we conducted mail surveys of 500 emergency physicians in each of these countries: Canada, United States, United Kingdom, France, and Spain. The majority of physicians in these countries indicated strong support for a CT head decision rule.

This study will develop guidelines for the use of CT in patients with minor head injury. The majority of head injuries seen in EDs can be classified as minor with a very low but definite rate of serious sequelae such as epidural hematomas. The current use of expensive diagnostic technology—CT scanning of the head—for these patients is very variable and inefficient. Furthermore, important cases of intracranial hematomas are being missed in patients sent home from EDs without a CT scan.

Current guidelines provide conflicting recommendations for the use of CT, and previous studies to develop guidelines have been methodologically weak and inconclusive. This study will build on our previous research in which we derived, validated, and successfully implemented decision rules for ankle radiography (Ottawa Ankle Rules) and for knee radiography (Ottawa Knee Rule). We recently also derived a rule for cervical spine radiography (Canadian Cervical Spine Rule). Reliable and sensitive decision rules permit physicians to be more accurate in their diagnosis of acute brain injury among patients with minor head injury and less likely to miss important intracranial hematomas. Furthermore, physicians could be more selective in their use of CT without jeopardizing the quality of patient care. Therefore, such decision rules should lead to improved patient care, as well as considerable savings for North American health care systems. We estimate that, depending on local practice, a 25% to 50% relative reduction in the use of CT could be safely achieved with a reliable decision rule.

The goal of phase I is to derive a clinical decision rule that is highly sensitive for detecting acute brain injury and will allow emergency physicians to maximize the efficiency of their use of CT scanning in patients with minor head injury. This will optimize patient care by ensuring that acute brain injury is identified among patients with minor head injury regardless of the hospital setting. By reducing or preventing the unnecessary use of CT, this decision rule also should lead to significant health care savings without jeopardizing quality of care for patients.

Specific Objectives for Phase I: Derivation of the Rule

1. To develop and pretest standardized clinical assessment methods for patients with acute minor head injury.
2. To apply these standardized clinical assessments to patients with acute minor head injury.
3. To determine the interobserver reliability of the clinical findings.
4. To determine the association between the clinical findings and acute brain injury.
5. To use multivariate techniques to derive a highly sensitive clinical decision rule for acute patients with minor head injury to guide the use of CT.
6. To assess the classification performance of the derived decision rule.
7. To determine emergency physicians’ comfort in ordering no CT.
8. To determine emergency physicians’ accuracy in predicting acute brain injury without the decision rule.

METHODS: PHASE I

Study population

Consecutive adult patients presenting to one of the study hospital EDs after sustaining acute minor head injury will be enrolled into the study. Eligibility as an “acute minor head injury” case will be determined by the attending physician based on the patient having all of the following characteristics on arrival in the ED: (1) blunt trauma to the head resulting in witnessed loss of consciousness, definite amnesia, or witnessed disorientation, no matter how brief; this may be determined from the patient or from the report of a witness (the patient will be asked specific questions: “do you remember the accident?”, “how did you get to the hospital?”, “have you talked to me before?”), (2) initial ED GCS score of 13 or greater as ascertained by the attending physician, and (3) injury within the past 24 hours; review of the pilot study data reveals that the majority of patients with minor head injury are seen within 24 hours of the injury.

Patients will be excluded from the study if they (1) are younger than 16 years, (2) have “minimal” head injury (ie, no loss of consciousness, amnesia, or disorientation), (3) are without a clear history of trauma as the primary event (eg, primary seizure or syncope), (4) have a GCS score of less than 13, (5) have a head injury that occurred more than 24 hours previously, (6) have obvious penetrating skull injury or depressed fracture, (7) have acute focal neurologic deficit (motor or cranial nerve) that cannot be ascribed to an extracerebral cause (eg, traumatic mydriasis or peripheral neuropathy), (8) have had a seizure before assessment in the ED, (9) have a bleeding disorder or currently use oral anticoagulants, (10) return for reassessment of the same head injury, or (11) are pregnant.

The research ethics committees of the study hospitals have approved the study without the need for informed consent at the time of enrollment. Patients who are followed up will have an opportunity to give verbal consent to the telephone interview by a study nurse. Normal patient management will not be altered (ie, patients will not be subjected to new therapy, invasive procedures, undue risk or discomfort, or use of diagnostic radiography beyond that which would normally be required in the course of patient care). CT scans will be ordered according to standard practice (ie, according to the clinical judgment of the treating physician). Patient confidentiality will be maintained throughout the study and patient names will be removed from all records.

Setting

The study setting will be 8 Canadian community and teaching institutions with a combined annual ED volume of approximately 400,000 patient visits. We believe that the generalizability of the derived rule will be by conducting the study in a large number of hospitals from different areas of Canada.

Standardized patient assessment

All patient assessments will be made by staff physicians who are certified in emergency medicine or by supervised residents in emergency medicine training programs. Other rotating residents may see eligible patients with head injuries but will be asked to have staff physicians make the study assessments. The physician assessors will be trained in 1-hour sessions to assess the clinical variables in a uniform manner. The physicians will record their findings on the data collection sheets before sending the patients for CT. There will be ongoing evaluation of the quality of the patient assessments judged by completeness of data sheets and compliance in enrolling eligible patients. Clinicians will be provided monthly feedback of a general nature and specific review of any individual problems that may arise.

The variables selected for assessment in the study were chosen by the investigators at the Research Formulation Workshop based on clinical experience and data from the literature. These variables are considered useful in predicting whether the patient with minor head injury has acute brain injury. The inclusion of too many variables in the protocol would increase the time required of the physician assessors and lead to decreased compliance
with the study. Several variables discussed in the literature were deemed to be not useful or feasible for this study. Therefore, the following variables will not be assessed: isease, dizziness, visual complaints, tinnitus, Reaction Level Scale, forward digit span recall, reverse digit span recall, tandem gait, facial injury, or scalp injury (hematoma, laceration, contusion, abrasion). The variables to be assessed are listed in Figure 2; the references indicate studies in which the variable was found to be significantly associated with acute brain injury.

The physicians also will be asked to answer 3 questions regarding their attitude to radiography and their clinical judgment: (1) theoretical comfort with ordering no CT for that patient, on a 5-point scale (very comfortable to very uncomfortable); (2) probability of acute brain injury, to the closest decile; and (3) probability of patient requiring neurologic intervention, to the closest decile.

**Figure 2.**
Standardized patient assessment.

<table>
<thead>
<tr>
<th>1. Variables from history</th>
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| a. **Age** 
8, 14, 28-30, 40, 49 |
| b. **Sex** |
| c. Mechanism of injury, classified in 21 categories 
13, 23, 28, 30, 40 |
| d. If motor vehicle crash, (i) speed, (ii) collision, (iii) seatbelt use, (iv) "bull's-eye" damage to windshield, (v) rollover, (vi) ejection, (vii) head-on collision, (viii) death in vehicle |
| e. If bicycle crash, helmet use |
| f. Witnessed loss of consciousness 
14, 103 |
| g. If yes, duration of loss of consciousness 
30 |
| h. **Amnesia** |
| i. If yes, duration of amnesia for period before injury and period after injury 
28, 30, 46 |
| j. Suspected chronic ethanol abuse |
| k. Time from injury to assessment in hours |

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<tr>
<th>2. Variables from neurologic examination</th>
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| a. Initial GCS score in ED 
11, 12, 14, 28, 30, 31, 40, 103 |
| b. Hourly GCS reassessments by nurse (time to reach a score of 15 will be specifically noted) |
| c. Object recall at 2 minutes (score out of 3 objects) |
| d. Pupillary changes 
28, 30 (anisocoria) |
| e. Lateralizing motor weakness 
11, 15, 30, 31, 46, 103 (arm drift, grip strength) |

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<tr>
<th>3. Variables from general examination or diagnostic tests</th>
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<tbody>
<tr>
<td>a. Repeated vomiting and number of episodes</td>
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<tr>
<td>b. Seizure while in ED</td>
</tr>
<tr>
<td>c. Suspected open skull fracture (suspected skull penetration or depressed fracture)</td>
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</table>
| d. Any sign of basilar skull fracture 
15, 30, 40 (drainage from ear, cerebrospinal fluid rhinorrhea, hemotympanum, Battle’s sign, “raccoon eyes”) |
| e. Acute ethanol or drug intoxication clinically suspected (to the extent that physical examination is unreliable) |
| f. Serum ethanol level 
46 (ordered if intoxication suspected) |
| g. Fracture on skull radiography 
3-15, 44 (radiography ordered if physician concerned about possible skull penetration or depressed fracture) |

The data collection sheets, patient assessment techniques, and patient follow-up questions will be evaluated and revised as necessary during a 2 month run-in period before the actual study. This period will also allow for time to train the physician assessors.

A subset of patients will be assessed for the clinical variables by a second emergency physician who will be blinded to the results of the first assessment. These second assessments will be performed in all centres on a feasibility basis whenever 2 study physicians are available in the ED.

**Outcome measures**

The primary outcome is “need for neurologic intervention,” which is defined as either (1) death resulting from head injury or (2) the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury. All patients admitted to the hospital will have their records reviewed by a research assistant who is unaware of the contents of the data collection sheet to determine whether death or neurologic intervention occurred.

“Clinically important brain injury” on CT is defined as any acute brain finding revealed on CT scanning and that would normally require admission to hospital and neurosurgical follow-up. This definition has been standardized based on the results of a formal survey of 129 academic neurosurgeons, neuroradiologists, and emergency physicians at 8 study sites. All brain injuries on CT are considered clinically important unless the patient is neurologically intact and has one of these lesions on CT: (1) solitary contusion less than 5 mm in diameter, (2) localized subarachnoid blood less than 1 mm thick, (3) smear subdural hematoma less than 4 mm thick, (4) isolated pneumocephaly, or (5) closed depressed skull fracture not through the inner table. Injuries will be classified as “clinically unimportant” after independent review of the CT scans by the study neurosurgeon and the study neuroradiologist. They will both be unaware of the contents of the data collection sheet and the other’s interpretation. Disagreements will be resolved by consensus.

Linear or basal skull fractures, in the absence of acute brain injury, generally do not require intervention and will be considered less important outcomes. Assessment of long-term outcomes, such as neuropsychological deficit, 91, 92 is considered beyond the scope of this study.

Patients will undergo standard CT scanning of the head after the clinical examination according to the judgment of the treating physician (ie, according to current
practice). Physicians will be explicitly cautioned not to order CT according to the decision rule. The CT scans will be interpreted by fully qualified independent staff neuroradiologists who will be provided routine clinical information but who will be blinded to the contents of the data collection sheet. The reliability of the radiography interpretations will be assessed during phase 1 by having all abnormal CT scans and 5% (randomly selected) of normal scans reviewed by a second radiologist who was blinded to the first interpretation. CT will be without contrast, will be performed with third-generation equipment, will involve cuts of 10 mm or less from the foramen magnum to the vertex, and will include both soft tissue and bone windows.

Because review of current practice at the study hospitals indicates variation from center to center and that many eligible patients with minor head injury routinely do not undergo CT scanning, we believe that the study protocol cannot ethically demand that all patients have CT scans. Generally, patients who are not referred for CT have less severe injuries and are very unlikely to have clinically significant brain injury. Nevertheless, all enrolled patients who do not have imaging will have telephone follow-up and will be classified as having no clinically important brain injury if they meet all the following explicit criteria at 14 days: (1) headache is absent or mild, (2) no complaints of memory or concentration problems, (3) have not had a seizure or developed focal motor findings, (4) weighted error score of no more than 10 out of 28 on the Katzman Short Orientation-Memory-Concentration Test (Figure 3), and (5) have returned to normal daily activities (work, housework, or school). The assessment of these criteria will be made by a research assistant who is unaware of the patient’s status for the individual predictor clinical variables. Patients who cannot fulfill these criteria will be recalled for clinical reassessment and CT scanning. This list of criteria was developed by the investigators based on their clinical judgment and is similar to criteria used in our previous ankle, knee, and cervical spine injury studies. The validity of these criteria to exclude acute brain injury has been confirmed during a substudy in which the telephone follow-up questionnaire was applied to a random sample of study patients with and without brain injury and who had all undergone CT scanning.

Data analysis

The interobserver agreement for each variable will be measured by calculating the \(\kappa\) coefficient, the proportion of potential agreement beyond chance, along with 95% confidence intervals (CIs).\cite{95,96} For variables with 3 or more ordered categories, a weighted \(\kappa\) measure of interobserver agreement will be calculated.\cite{97} A variable will be deemed to have acceptable interobserver agreement if the \(\kappa\) coefficient has a value of at least 0.6. The value of 0.6 is considered to represent “substantial agreement”\cite{95,96} and has proven to be a satisfactory threshold in our previous research for ankle and knee decision rules.

Univariate analyses will be used to determine the strength of association between each variable and the primary outcome, need for neurologic intervention, and the secondary outcome, clinically important brain injury. This process will aid selection of the best variables for the multivariate analyses. The appropriate univariate technique will be chosen according to the type of data: for nominal data, the \(\chi^2\) test with continuity correction; for ordinal variables, the Mann-Whitney \(U\) test; and, for continuous variables, the unpaired 2-tailed \(t\) test, using pooled or separate variance estimates as appropriate.

Multivariate analyses will derive a model to predict the primary and secondary outcomes. Those variables found to be both reliable (\(\kappa>0.6\)) and strongly associated with the outcome measures (\(P<.05\)) will be combined using 1 of 2 different multivariate techniques, recursive partitioning or logistic regression. Second-order interaction among predictor variables will be evaluated using the Mantel-Haenszel and logistic model procedures and appropriate composite variables will be considered for incorporation into the multivariate analyses.

The objective will be to find the best combinations of predictor variables that are highly sensitive for detecting the outcome measure while achieving the maximum pos-

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<tr>
<th>Items</th>
<th>Maximum Error</th>
<th>Score</th>
<th>Weight</th>
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<tbody>
<tr>
<td>1. What year is it now?</td>
<td>1</td>
<td>4</td>
<td>=</td>
</tr>
<tr>
<td>2. What month is it now?</td>
<td>1</td>
<td>3</td>
<td>=</td>
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Memory Phrase:

Repeat this phrase after me:

John Brown, 42 Market Street, Chicago

3. About what time is it? (within 1 h) | 3 | = |
| 4. Count backwards 20 to 1 | 2 | 2 | = |
| 5. Say the months in reverse order | 2 | 2 | = |
| 6. Repeat the memory phrase | 2 | 2 | = |

Score of 1 for each incorrect response; maximum weighted error score=24.
sible specificity. To be clinically acceptable, the model must be nearly 100% sensitive. The derived models must be easy to use by clinicians and therefore should contain as few variables as possible. Therefore, a model will only be acceptable if it fulfills these criteria: (1) 99% or greater sensitivity, (2) adequate specificity to lead to a 20% relative reduction in use of CT, and (3) no more than 8 component variables. Assuming more than one model meets the minimum acceptable criteria, the best model will be the one that has the highest specificity and the fewest number of component variables.

Recursive partitioning will be used to determine the most significant variables in a model highly sensitive for the primary outcome measure and will be performed using KnowledgeSEEKER software (version 3.0; Angoss Software International, Toronto, Ontario, Canada).\textsuperscript{98-101} We have had extensive experience in using recursive partitioning to develop decision rules for ankle and for knee injury radiography. Our experience suggests that recursive partitioning may be more suitable than logistic regression when the objective is to correctly classify one outcome group at the expense of the other (i.e., where high sensitivity is more important than overall accuracy). We can deliberately drive the analysis to correctly classify the “need neurologic intervention” group at the expense of the group with no injury. We can also deliberately avoid complex models with significant interactions that would be difficult for clinicians to interpret or apply.

Attempts will also be made to find the best model by performing logistic regression as an alternate multivariate technique to recursive partitioning. Model building will proceed with forward stepwise selection until no variables meet the entry (0.05) or removal (0.10) criteria for the significance level of the likelihood ratio test. To provide a simpler model for clinicians, cutpoints will be sought for continuous variables. Variables selected for the model will be given weights equal to the coefficient rounded to the nearest whole number. We have successfully applied a similar approach to developing a decision rule for delayed functional recovery in patients with knee injury.

The variables chosen by the best model will constitute the decision rule for selecting patients with minor head injury for CT scanning. The decision rule will be presented in clear narrative form that does not require computation or use of statistical aids.

The derived decision rule will be cross-validated by comparing the classification of each patient with their actual status for the primary and secondary outcomes. This will allow an estimate, with 95% CIs, of the sensitivity and specificity of the rule. A more robust validation will be carried out prospectively on a new set of patients in phase II.

Data from the 3 questions on physicians’ comfort and predictions will be tabulated in a simple descriptive format. In addition, information on the predicted probabilities will be used to calculate receiver operating characteristic (ROC) curves and likelihood ratios for determining acute brain injury, as well as the need for neurologic intervention, respectively. The accuracy of the physicians’ predictions will be compared with that of the derived decision rule by ROC curve analysis.

**Sample size**

A total of 2,500 patients will be enrolled over 30 months at the study sites. Because no hypothesis is being tested, sample size is based on estimation of the precision of the sensitivity of the derived decision rule. The sample size must accommodate the very low prevalence of cases requiring neurologic intervention (estimated to be 1.6% of patients enrolled) or having important brain injury (8.7%). A sample size of 2,500 eligible patients with minor head injury should yield approximately 40 cases requiring neurologic intervention and 230 cases with important brain injury. For a 100% sensitivity, this sample size would yield upper and lower limits of the 95% CIs of 100% to 91%, respectively, for neurologic intervention and 100% to 98% for important brain injury.\textsuperscript{97} Furthermore, for a cumulative sensitivity of 100% in phases I and II combined, the 95% CI limits would be 100% to 95% for 80 cases of neurologic intervention and 100% to 99% for 460 cases of important brain injury.

We will have 200 patients assessed by 2 study physicians to determine interobserver agreement. The number 200 is dictated primarily by considerations of feasibility as obtaining assessments by 2 physicians in a busy ED is very difficult. With 200 patients, the upper and lower limits for a $\kappa$ value of 0.6 are 0.73 and 0.47, respectively.\textsuperscript{102}

**Phase II: Prospective Validation**

The methodology for phase II (prospective validation and preliminary economic analysis) will be presented in the subsequent part II article in the September 2001 issue of *Annals of Emergency Medicine*.\textsuperscript{103} The results of phase I have been recently published.\textsuperscript{104}

**References**

77. McDonald CJ. Guidelines you can follow and can trust: an ideal and an example. JAMA. 1994;271:872-873.