Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department with Mild Traumatic Brain Injury

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From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Mild Traumatic Brain Injury:

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ABSTRACT

This 2022 Clinical Policy from the American College of Emergency Physicians is an update of the 2008 "Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting." A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following questions: 1) In the adult emergency department patient presenting with minor head injury, are there clinical decision tools to identify patients who do not require a head computerized tomography? 2) In the adult emergency department patient presenting with minor head injury, a normal baseline neurological examination, and taking an anticoagulant or anti-platelet medication, is discharge safe after a single head computed tomography? and 3) In the adult emergency department patient diagnosed with mild traumatic brain injury or concussion, are there clinical decision tools or factors to identify patients requiring follow-up care for post-concussive syndrome or to identify patients with delayed sequelae after emergency department discharge? Evidence was graded and recommendations were made based on the strength of the available data. Widespread and consistent implementation of evidence-based clinical recommendations is warranted to improve patient care.

INTRODUCTION

Traumatic brain injuries (TBIs) affect the lives of millions of Americans and represent a serious healthcare challenge for emergency department (ED) clinicians nationwide.[1] A TBI is caused by an external force to the head or body or a penetrating injury to the head[2] and is associated with a wide-range of functional short- or long-term changes that may affect cognition (eg, memory and reasoning), sensation (eg, sight and balance), language (eg, communication and understanding); and/or emotion (eg, depression, personality changes).[3] The initial severity of a TBI may range from "mild," ie, a brief change in mental status or consciousness to "severe," ie, an extended period of unconsciousness or amnesia after the injury.[3]

In one year alone, EDs in the United States manage more than 25 million injury-related visits, including those for patients with a suspected TBI.[4] There were approximately 223,050 TBI-related hospitalizations in 2018 and 60,611 TBI-related deaths in 2019 in the United States.[5] Recent data indicates that most TBIs occur among adults, with adults age 75 years and older accounting for approximately 32% of TBI-related hospitalizations and

28% of TBI-related deaths.[5] Current data may underestimate the true burden of this injury as people who do not seek medical care after a head injury and patients seen in outpatient, federal, military, or the United States Department of Veterans Affairs (VA) settings may not be included in published reports. Racial and ethnic minorities,[6] people who experience homelessness,[7] people who are in correctional and detention facilities,[8] and survivors of intimate partner violence[9] are groups disproportionately affected by TBI. Moreover, people living in rural areas have higher TBI-related mortality rates as compared to people living in urban areas.[10-12] Explanations for this disparity may include greater distance to emergency medical care,[13] limited access to a Level I trauma center within 1 to 2 hours of the injury,[14] differing mechanism of injury,[6] and difficulty obtaining specialized TBI care.[15] While rates vary by group, overall, suicide (most firearm-related) followed by unintentional falls, and unintentional motor vehicle crashes are the leading mechanisms of TBI-related deaths in the United States.[5,6] Unintentional falls are the leading mechanism of TBI-related hospitalizations in the United States.[5]

Approximately 70% to 90% of patients with a head injury and TBI presenting to the ED will be diagnosed as having a mild traumatic brain injury (mTBI).[16,17] A mTBI is associated with neuronal dysfunction involving a cascade of ionic, metabolic, and physiologic events.[18-21] This cascade, as well as microscopic axonal dysfunction, may lead to acute clinical signs and symptoms that evolve during recovery.[3,21] In 2004, the World Health Organization (WHO) Collaborating Centre Task Force on mTBI, the mTBI Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine (ACRM) and the United States Centers for Disease Control and Prevention (CDC) defined mTBI as "an acute brain injury resulting from mechanical energy to the head from external physical forces including: (1) 1 or more of the following: confusion or disorientation, loss of consciousness (LOC) for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, symptoms, or seizure; (2) Glasgow Coma Scale (GCS) score of 13 to 15 after 30 minutes postinjury or later upon presentation for healthcare."[22,23] While most patients with mTBI will be treated and discharged from an ED,[24] an estimated 5% to 15% of patients will have intracranial injuries on imaging.[25] Roughly 1% of these patients will require surgical intervention and fewer will die (0.1%).[25,26]

The costs for all severity levels of TBI are not purely limited to economics. Costs are multifactorial and include dynamic societal, psychosocial, physical, mental, medicolegal, and other quality of life factors that are

often challenging to quantify. Further complicating this is the fact that TBI is not solely an acute problem. According to CDC, the lifetime economic cost of TBI, including direct and indirect costs, was $76.5 billion in 2010 United States dollars.[27] While most patients presenting to the ED with mTBI are asymptomatic within a couple of weeks, some patients will have persistent symptoms requiring further care and added expenses.[16,17,28] A 12-month analysis of health care utilization following the diagnosis of mTBI in the United States in 80,004 patients reported mean costs of $13,564 (SD=$41,071) involving a combination of inpatient and outpatient services.[29] Prevention and appropriate management of mTBI is critical to reducing the economical and societal burden on the lives of Americans.

Rationale for the clinical questions in the 2022 ACEP Clinical Policy

As variation in mTBI diagnosis and management practices in the United States may contribute to disparities in patient outcomes, widespread and consistent implementation of evidence-based clinical recommendations is warranted.[10,30] To this end, in 2008, the American College of Emergency Physicians (ACEP) Clinical Policy Committee published and disseminated the *Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting* (2008 Clinical Policy).[31] As research on mTBI has continued to evolve and emerge since 2008, the ACEP Clinical Policy Committee conducted an updated systematic review of the literature to assess any needed changes to the 2008 Clinical Policy and to determine whether there was a need for additional evidence-based recommendations. The Committee determined that the recommendations made in the 2008 Clinical Policy were still relevant and did not warrant revision. However, the Committee identified emergent mTBI research related to clinical decision tools, patients using anticoagulant or anti-platelet medication, and post-concussion syndrome that was sufficient to merit clinical application. This document, *Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department with Mild Traumatic Brain Injury* (2022 ACEP Clinical Policy), is the result of these efforts. The 2022 ACEP Clinical Policy is comprised of three clinical questions: 1) In the adult ED patient presenting with minor head injury, are there clinical decision tools to identify patients who do not require a head computed tomography (head CT)?; 2) In the adult ED patient presenting with minor head injury, a normal baseline neurological examination, and taking an anticoagulant or anti-platelet medication, is discharge safe after a single

head CT?; and 3) In the adult ED patient diagnosed with mTBI or concussion, are there clinical decision tools or factors to identify patients requiring follow-up care for post-concussive syndrome (PCS) or to identify patients with delayed sequelae after ED discharge?

In part due to heterogeneity within the literature in enrolled patient populations, research definitions, and outcomes, there is some inconsistency within studies to determine the need for head CT in patients with suspected mTBI. In order to provide better insight, we included key word definitions to common terms used throughout the literature to allow for consistency and clarity (Appendix A). Heterogeneity in the literature has led to challenges in creating evidence-based guidelines on CT usage.[16] However, research on this topic has expanded in recent years. As such, the first clinical question examined in this 2022 ACEP Clinical Policy addresses head CT usage and is the reciprocal of the first question in the 2008 ACEP Clinical Policy. In 2008, the question asked, "which patients with mTBI should have a non-contrast head CT in the ED?"[31] The updates to this first question were designed to pair with the *Choosing Wisely*® campaign. Created by the American Board of Internal Medicine (ABIM), *Choosing Wisely*® promotes utilization of evidence-based care practices facilitated by improving conversations between clinicians and patients with shared decision-making.[32] Based on the work of an ACEP task force in 2013, 10 items were identified for inclusion in the *Choosing Wisely*® campaign. The first item recommended clinicians: "Avoid CT scans of the head in ED patients with minor head injury who are at low risk based on validated decision rules."[32] This recommendation is consistent with current research and considered an actionable target to improve healthcare value of services delivered, reduce unnecessary procedures and exposure to radiation for patients, and improve direct medical costs.[33]

Coinciding with the aging of the United States population, the number of patients taking anticoagulation and antiplatelet therapies has also risen substantially.[34,35] While these medications afford benefits to patients with serious health conditions, research suggests that they may complicate TBI diagnosis and management.[36] As such, the second clinical question in this 2022 ACEP Clinical Policy addresses the safety of discharging a patient with mTBI taking anticoagulants or anti-platelet medications from the ED following an initial head CT.[35,37] Finally, as evidence concerning the potential for long-term physical, cognitive, and mental health problems following mTBI expands,[28] the third question, takes into account the challenge of identifying patients diagnosed with mTBI or

concussion who may be at increased risk for PCS or subsequent negative sequalae that requires specialized follow-up care after ED discharge.

Defining mild TBI Controversy

Despite being a common injury, there is significant discrepancy in the literature and among medical societies regarding the definition of mTBI and no consensus definition for mTBI currently exists. Various government and medical societies have sought to define mTBI including the following: ACRM; American College of Occupational and Environmental Medicine (ACOEM); Brain Trauma Foundation (BTF); CDC; American College of Sports Medicine (ACSM); American Medical Society for Sports Medicine (AMSSM); WHO; International Conference on Concussion in Sport; National Academy of Medicine (NAM), formerly called the Institute of Medicine (IOM); American Academy of Neurology (AAN); Eastern Association for the Surgery of Trauma (EAST); Ontario Neurotrauma Foundation (ONF), and ACEP. All have used varying definitions and there is debate regarding whether the term concussion is synonymous with mTBI or if concussion is a subset of mTBI. In the published literature, concussion, mild or minor head trauma, and mild head injury are often used interchangeably.[17,38] The Ontario Neurotrauma Foundation Concussion/mTBI Guideline published in 2018 noted that, "all concussions are considered to be a mTBI, however mTBI is distinguished from concussion when there is evidence of intracranial injury on conventional neuroimaging or there is persistent neurologic deficit."[39] The WHO defined these separately and their definition of mTBI also includes intracranial injury not requiring surgery.[40] However, many practicing clinicians would not necessarily agree that positive findings on imaging would equate to a "mild" TBI. In patients with a GCS 13, which many define as mTBI, there have been reports of a higher incidence of injuries requiring surgical intervention, and in subsets of mTBI with a GCS 13 and intraparenchymal lesions, patients have reportedly performed poorer on neuropsychological evaluations more consistent with those in moderate TBI groups.[31,41,42] One author, Stein, even titled a report as "Minor Head Injury: 13 is an Unlucky Number" in reference to the increased problems associated with a GCS 13.[41] The VA and Department of Defense (DoD) definition of mTBI and concussion from 2016, which is currently under revision, includes normal structural imaging if obtained.[43] In the 2015 CDC Report to Congress, mTBI is referenced to include normal structural imaging, LOC <30 minutes, post-traumatic amnesia 0 to 1 day, and GCS 13 to 15.[44] The

CDC report also acknowledged that use of GCS alone can lead to misclassification of TBI and even individual characteristics of severity criteria (ie, for mild, moderate, or severe), when used alone, cannot accurately predict severity and outcomes.[44,45] The VA/DoD's most updated version of its definition of TBI no longer recommended the use of GCS to diagnose TBI.[43] Since there is no universal definition for mTBI, we chose to stay consistent with the ACEP 2008 adult mTBI clinical policy by including only blunt head injury patients age 16 years or older with a GCS 14 or 15 and improvement to GCS 15 at 2 hours post injury if initial GCS 14 with or without a history of the following: LOC, amnesia, or disorientation presenting for evaluation within 24 hours.[31] GCS 13 will not be considered mTBI since many experts and authors note a higher or moderate risk in this group as previously discussed (See mTBI in Definitions Appendix A). In this 2022 ACEP Clinical Policy, the term mTBI and concussion may be used interchangeably unless otherwise stated. The articles were graded and interpreted based upon how mTBI was defined by the authors. Most patients in the studies examined for this guideline had a GCS 14 or 15. However, when the studies included patients with GCS 13, this was addressed in the prose.

METHODOLOGY

This ACEP clinical policy is based on a systematic review and critical descriptive analysis of the medical literature and is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[46]

Search and Study Selection

This clinical policy is based on a systematic review with critical analysis of the medical literature meeting the inclusion criteria. Searches of PubMed, SCOPUS, Embase, Web of Science, and the Cochrane Database of Systematic Reviews were performed by a librarian. Search terms and strategies were peer reviewed by a second librarian. All searches were limited to human studies published in English. Specific key words/phrases, years used in the searches, dates of searches, and study selection are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Two subcommittee members independently read the identified abstracts to assess them for possible inclusion. Of those identified for potential inclusion, each full-length text was reviewed for eligibility. Those identified as eligible were subsequently forwarded to the committee's methodology group (emergency physicians with specific research methodological expertise) for methodological grading using a Class of Evidence framework (Appendix B).

Assessment of Risk of Bias and Determination of Classes of Evidence

Each study identified as eligible by the subcommittee was independently graded by two methodologists. Grading was done with respect to the specific critical questions; thus, the Class of Evidence for any one study may vary according to the question for which it is being considered. For example, an article that is graded an "X" due to "inapplicability" for one critical question may be considered perfectly relevant for another question and graded I – III. As such, it was possible for a single article to receive a different Class of Evidence grade when addressing a different critical question.

Design 1 represents the strongest possible study design to answer the critical question, which relates to whether the focus was therapeutic, diagnostic, or prognostic, or a meta-analysis. Subsequent design types (ie, Design 2 and Design 3) represent respectively weaker study designs. Articles are then graded on dimensions related to the study's methodological features and execution, including but not limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, generalizability, data management, analyses, congruence of results and conclusions, and potential for conflicts of interest.

Using a predetermined process that combines the study's design, methodological quality, and applicability to the critical question, two methodologists independently assigned a preliminary Class of Evidence grade for each article. Articles with concordant grades from both methodologists received that grade as their final grade. Any discordance in the preliminary grades was adjudicated though discussion which involved at least one additional methodologist, resulting in a final Class of Evidence assignment (ie, Class I, Class II, Class III, or Class X) (Appendix C). Studies identified with significant methodologic limitations and/or ultimately determined to not be applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating

recommendations for this policy. However, content in these articles may have been used to formulate the background and to inform expert consensus in the absence of evidence. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Based on the strength of evidence for each critical question, the subcommittee drafted the recommendations and supporting text synthesizing the evidence using the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of scientific certainty (eg, based on evidence from one or more Class of Evidence I, or multiple Class of Evidence II studies that demonstrate consistent effects or estimates).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate scientific certainty (eg, based on evidence from one or more Class of Evidence II studies, or multiple Class of Evidence III studies that demonstrate consistent effects or estimates).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as consistency of results, uncertainty of effect magnitude, and publication bias, among others, might lead to a downgrading of recommendations. When possible, clinically-oriented statistics (eg, likelihood ratios [LRs], number needed to treat) are presented to help the reader better understand how the results may be applied to the individual patient. This can assist the clinician in applying the recommendations to most patients but allow adjustment when applying to patients with extremes of risk (Appendix D).

Evaluation and Review of Recommendations

Once drafted, the policy was distributed for internal review (by members of the entire committee) followed by external expert review and an open comment period for all ACEP membership. Comments were received during a 60-day open comment period with notices of the comment period sent electronically to ACEP members, published in *EM Today*, posted on the ACEP Web site, and sent to other pertinent physician organizations. The responses were used to further refine and enhance this clinical policy, although responses do not imply endorsement. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology, methodology, or the practice environment changes significantly.

Application of the Policy

This policy is not intended to be a complete manual on the evaluation and management of adult patients with mTBI but rather a focused examination of critical questions that have particular relevance to the current practice of emergency medicine. Potential benefits and harms of implementing recommendations are briefly summarized within each critical question.

It is the goal of the Clinical Policies Committee to provide evidence-based recommendations when the scientific literature provides sufficient quality information to inform recommendations for a critical question. When the medical literature does not contain adequate empirical data to inform a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline provides clinical strategies for which medical literature exists to inform the critical questions addressed in this policy. ACEP funded this clinical policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. The guideline is intended for adults with blunt head injury (Q1/Q2), or adults diagnosed with mild traumatic brain injury or concussion (Q3).

Exclusion Criteria. This guideline is not intended for patients with a history of a bleeding disorder, pregnant patients, patients with a primary presentation of a seizure disorder, pediatric patients, patients with an obvious open or penetrating head injury, or patients with unstable vital signs with multi-system trauma.

CRITICAL QUESTIONS

1. In the adult ED patient presenting with minor head injury, are there clinical decision tools to identify patients who do not require a head CT?

Patient Management Recommendations

Level A recommendations. Use the Canadian CT Head Rule (CCHR) to provide decision support and improve head CT utilization in adults with minor head injury.

Level B recommendations. Use the NEXUS Head CT decision tool (NEXUS Head CT) or the New Orleans Criteria (NOC) to provide decision support in adults with minor head injury; however, the lower specificity of the NEXUS Head CT and NOC compared to CCHR may lead to more unnecessary testing.

Level C recommendations. Do not use clinical decision tools to reliably exclude the need for head CT in adult patients with minor head injury on anticoagulation therapy or antiplatelet therapy exclusive of aspirin.

Table 1. Clinical decision tools.

	Canadian CT Head Rule[47]	New Orleans Criteria[48]	NEXUS Head CT[49]
High risk features for predicting patients with CIBI	Any one of: • Failure to reach GCS of 15 within 2 hours of injury • Suspected open skull fracture • Signs of basal skull fracture • Vomiting more than once • Age greater than 64 years	Any one of: • Headache • Vomiting • Age over 60 years • Drug or alcohol intoxication • Deficits in short-term memory • Physical evidence of trauma above the clavicles • Post-traumatic seizure	Any one of: • Evidence of skull fracture • Scalp hematoma • Neurologic deficit • Abnormal level of alertness • Abnormal behavior • Persistent vomiting • Coagulopathy • Age 65 or greater
Exclusion Criteria	• Age <16 years • Blood thinners • Seizure after injury	• GCS <15 • Age ≤3 years	• GCS <15

CIBI, clinically important brain injury; *CT,* computed tomography; *GCS*, Glasgow Coma Scale.

Resources:

- Canadian CT Head Rule:[47] https://www.mdcalc.com/canadian-ct-head-injury-trauma-rule
- New Orleans/Charity Head Trauma/Injury Rule:[48] https://www.mdcalc.com/new-orleans-charity-head-trauma-injury-rule
- NEXUS Head CT:[49] https://bit.ly/NEXUSHeadCT

Potential Benefit of Implementing the Recommendations:

- Decreased costs and decreased radiation exposure due to potential for fewer head CT scans.

Potential Harm of Implementing the Recommendations:

- To the extent that decision rules lack specificity, there is potential for increased radiation to patients from unnecessary CT scans as well as increased healthcare costs and resource utilization. It is important to apply the available decision tools only to the appropriate patient population, as defined by inclusion and exclusion criteria of the studies. Inappropriate application can lead to both over-triage and unnecessary CT use, as well as under-triage and missed injuries. Additionally, identification of injuries that are not clinically important may lead to unnecessary additional downstream medical care costs and hospitalizations.

Key words/phrases for literature searches: brain concussion, brain injury, closed head injury, concussion, commotio cerebri, craniocerebral trauma, head injury, head trauma, instrument, mild traumatic brain injury, mTBI, minor head injury, traumatic brain injury, biological marker, biomarker, clinical assessment tool, clinical decision, clinical decision instrument, clinical decision tool, clinical decision rule, clinical prediction instrument, clinical prediction tool, clinical prediction rule, cognitive aid, decision support instrument, decision support system, decision support technique, screening aid, rule, screening tool, tool, brain computed tomography, brain CT, brain imaging, head computed tomography, head CT, multidetector computed tomography, x-ray computed tomography, and variations and combinations of the key words/phrases. Searches included January 2010 to search dates of January 16 and 21, and March 9 and 11, 2020.

Study Selection: One thousand one hundred sixty-three articles were identified in the searches. Twenty-four articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, zero Class I studies, 5 Class II studies, and 5 Class III studies were included for this critical question (Appendix E).

In the current practice of emergency medicine, clinical decision tools have become more commonplace in the attempt to improve patient safety and encourage responsible resource utilization. One area that has seen considerable research in developing clinical decision tools is minor traumatic head injury. The 2 most well studied and well validated are the Canadian CT Head Rule (CCHR) as initially developed by Stiell et al[47] in 2001, and the New Orleans Criteria (NOC), developed at Charity Hospital by Haydel et al[48] in 2000. These and other clinical decision tools tend to have similar components that can help physicians recognize high-risk patients.

Informed by prior studies that were primarily based on trauma registry data, 2 foundational studies were published in the early 2000s that led to a more robust validation of both the CCHR and NOC. Stiell et al,[47] in a

Class II study, performed a derivation and internal validation study prospectively evaluating 3,121 patients aged 16 years or older who had minor head injury, an initial ED GCS of 13 to 15 plus either witnessed LOC, definite amnesia, or witnessed disorientation. Exclusion criteria included the following: no clear trauma history (ie, primary seizure or syncope), obvious penetrating skull injury or depressed skull fracture, acute focal neurological deficit, unstable vital signs from trauma, seizure before ED assessment, bleeding disorder or use of oral anticoagulants, patients returning for repeat assessment of same injury, or pregnancy. Patients were assessed for 22 standardized clinical findings based on history and examination. The primary outcome measure was the need for neurosurgical intervention, and the secondary outcome was clinically important brain injury (CIBI). Need for neurological intervention was defined by the following: death within 7 days due to head injury or the need for any procedures within 7 days (eg, craniotomy, skull fracture elevation, intracranial pressure monitoring, or intubation for head injury shown on head CT). Clinically important brain injury was defined as any acute intracranial finding revealed on CT that would normally require admission to the hospital and neurological follow-up. Sixty seven percent (2,078 of 3,121) of the patients had a CT to assess secondary outcomes, but surrogate measures, including telephone follow-up with neurologic assessment, were used in place of a negative CT to assess primary outcome measures. In patients that were neurologically intact, clinically unimportant lesions included solitary contusions less than 5 mm in diameter, localized subarachnoid blood less than 1 mm thick, smear subdural hematomas less than 4 mm thick, isolated pneumocephaly, or closed depressed skull fractures not through the inner table. A set of high-risk and medium-risk factors was developed, and the high-risk factors were 100% sensitive (95% CI 92% to 100%) and 68.7% specific (95% CI 67% to 70%) for predicting need for neurological intervention which would have required only 32.2% of patients to undergo CT. The medium-risk factors were 98.4% sensitive (95% CI 96% to 99%) and 49.6% specific (95% CI 48% to 51%) for predicting CIBI which would have required only 54.3% of patients to undergo CT. The authors concluded that CT in minor head injury is indicated in patients with 1 of 5 high-risk factors: failure to reach a GCS score of 15 within 2 hours of injury, suspected open skull fracture, sign of basal skull fracture, vomiting more than once, or age greater than 64 years.

Similarly, a Class III study from Haydel et al[48] in 2000 prospectively assessed patients with minor head injury to develop high risk features and validated these components in what is commonly known as the NOC. The authors included 1,429 patients who presented to the ED after minor head injury with GCS of 15, a normal brief

neurological exam (ie, normal cranial nerves, normal strength and sensation of arms and legs), and a history of LOC or amnesia. Exclusion criteria included the following: patients who declined CT, concurrent injuries precluding use of CT, or patients reporting no LOC or amnesia for the traumatic event. In the derivation phase, 520 patients were included and 6.9% (95% CI 4.2% to 9.6%) had an abnormal CT. The CT was considered abnormal if it showed an acute traumatic intracranial lesion (ie, a subdural, epidural, or parenchymal hematoma; subarachnoid hemorrhage; cerebral contusion; or depressed skull fracture). In the validation phase, 909 patients were included and 6.3% (95% CI 4.7% to 7.8%) had a positive CT. All patients with a positive CT had one or more of 7 findings: headache, vomiting, age over 60 years, drug or alcohol intoxication, deficits in short-term memory, physical evidence of trauma above the clavicles, and post-traumatic seizure. In this group, the sensitivity of these 7 factors was 100% (95% CI 95% to 100%) and the specificity was 25% (95% CI 22% to 28%).

Apart from the CCHR and the NOC, the NEXUS Head CT decision instrument (NEXUS Head CT) has additionally shown promise as a clinical decision tool. First proposed in 2002, Mower et al[49] completed the 10-year prospective observational study in 2015. Subsequently, Mower et al[49] published the Class II study in 2017 evaluating 8 high risk criteria (ie, evidence of skull fracture, scalp hematoma, neurologic deficit, abnormal level of alertness, abnormal behavior, persistent vomiting, coagulopathy, and age 65 or greater) that were applied to patients 16 years and older presenting to the ED with blunt head trauma that underwent head CT. Exclusion criteria included the following: patients with penetrating trauma, presentation >24 hours after injury, patients undergoing imaging unrelated to trauma, or those patients transferred with known intracranial injuries. Patients with the absence of all 8 criteria were considered at low risk of intracranial injury and deemed safe to omit from head CT imaging, while patients meeting 1 or more of the criteria were considered high risk. All ED patients with acute blunt head trauma that received a head CT were eligible. The ordering physicians were cautioned from using decision tools as a sole determinant and the ultimate decision to omit or perform imaging was made by the treating provider (not by study protocol). To account for verification bias, the study performed 3-month follow-up on a cohort of 368 consecutive patients with blunt head injury that had not been imaged to assess the potential effects. The primary outcome was need for neurosurgical intervention and the secondary outcome was CIBI using the same definition as Steill et al[47] (2001). For this study, 11,770 patients were enrolled with completed imaging and 420 required neurosurgical intervention. The NEXUS Head CT identified all 420 high-risk patients requiring

neurosurgical intervention demonstrating a sensitivity of 100% (95% CI 99.1% to 100%) and a specificity of 24.9% (95% CI 24.1% to 25.7%). Sensitivity and specificity for high-risk patients with CIBI was 99% (95% CI 98% to 99.6%) and 25.6% (95% CI 24.8% to 26.4%), respectively. The NEXUS Head CT correctly assigned low-risk status to 2,823 of 11,350 patients not requiring neurosurgical intervention (specificity 24.9% [95% CI 24.1% to 25.7%]). None of the 2,823 required intervention resulting in a negative predictive value (NPV) of 100% (95% CI 99.9% to 100%). The NEXUS Head CT correctly assigned low-risk status to 2,815 of 11,003 without significant intracranial injury (specificity 25.6% [95% CI 24.8 to 26.4%]). In patients deemed low risk by the NEXUS Head CT, significant injuries were not present in 2,815 of 2,823 resulting in a NPV of 99.7% (95% CI 99.4% to 99.9%). Mower et al[49] (2017) then further compared this NEXUS Head CT study group population with patients also meeting CCHR inclusions and exclusions (N=7,759 patients). The NEXUS Head CT had good sensitivity but was much less specific than the CCHR (Table 2).

Subsequently, several studies have evaluated the performance of both the CCHR and NOC in a variety of settings.[50-53] In a Class II study from 2005, Stiell et al[50] applied these 2 decision tools to a prospective cohort in 9 Canadian community and academic EDs. In this study, 1,822 patients with GCS 15 were included and the CCHR and the NOC both had 100% sensitivity (95% CI 63% to 100%) for predicting need for neurosurgical intervention. However, the CCHR was more specific at 76.3% (95% CI 74% to 78%) versus 12.1% (95% CI 11% to 14%) for NOC. Similarly, for CIBI, the CCHR and the NOC had similar sensitivity (100% versus 100%; 95% CI 96% to 100%), but again the CCHR was more specific at 50.6% (95% CI 48% to 53%) versus 12.7% (95% CI 11% to 14%) for NOC. In patients with GCS 15, the CCHR showed improved rates of CT usage versus NOC respectively; (CCHR 52.1% [95% CI 50% to 54%] versus NOC 88% [95% CI 86% to 89%]).

A Class II study by Smits et al[51] examined the CCHR and NOC at 4 university hospitals in the Netherlands. The decision tools were applied to 3,181 consecutive adult patients along with an adaptive model in patients with a GCS score of 13 to 14 or a GCS of 15 plus 1 of the risk factors identified by the decision rules. Neurosurgical intervention occurred in 17 patients (0.5%), and clinically important CT findings (any intracranial traumatic CT finding or depressed skull fracture) were present in 243 patients (7.6%). The original CCHR had a sensitivity for identifying neurosurgical intervention of 100% (95% CI 64.6% to 100%) and a specificity of 37.2% (95% CI 34.1% to 40.4%), while the original NOC had a sensitivity of 100% (95% CI 34.2% to 100%) and a

specificity of 5.3% (95% CI 2.5% to 8.3%). For the identification of a clinically important CT finding, the CCHR had a sensitivity of 84.5% (95% CI 78.1% to 89.3%) and a specificity of 38.9% (95% CI 35.6% to 42.3%), while the NOC had a sensitivity of 97.7% (95% CI 92.1% to 99.4%) and a specificity of 5.5% (95% CI 2.6% to 8.7%). In this study, the discrepancy between the sensitivities for the NOC and CCHR for clinically important CT findings is most likely due to a more demanding or comprehensive definition for external injury defined in the NOC compared with a more overall potentially severe definition with CCHR which does not allow for inclusion of findings such as minor abrasions. Additionally, Smits et al[51] defined "clinically important CT finding" differently by including "any intracranial traumatic finding" on CT such as depressed skull fractures. In contrast, the 2005 Stiell et al[50] study did not consider the following as clinically important: neurologically intact patients with any one of the following: 1) solitary contusion <5 mm, 2) localized subarachnoid hemorrhage (SAH) <1 mm, smear subdural hematoma (SDH) <4 mm, or closed depressed skull fracture (*not through the inner table).

A Class II systematic review by Easter et al[25] in 2015 examined the accuracy of symptoms and signs in adults with minor head trauma to identify those with severe intracranial injuries. Included in this systematic review were specific pooled data from 14 studies involving 23,079 patients with a prevalence of severe intracranial injury of 7.1% (95% CI 6.8% to 7.4%) and death or need for neurosurgical intervention of 0.9% (95% CI 0.78% to 1%). In patients with minor head injury with LOC, amnesia, or disorientation, the CCHR demonstrated a sensitivity of 99% (95% CI 78% to 100%) and specificity of 40% (95% CI 34% to 46%) for severe intracranial injury. In the same patient population, the NOC had a sensitivity of 99% (95% CI 90% to 100%) and specificity of 13% (95% CI 8.1% to 22%). Absence of all features of the CCHR lowered the probability of a severe intracranial injury to 0.31% (95% CI 0% to 4.7%) when accounting for the pooled study prevalence of 7.1%. Similarly, in the absence of all features of the NOC, the probability was 0.61% (CI 95% 0.08% to 6%).

In a Class III study by Ro et al,[52] 7,131 consecutive patients were enrolled in a prospective cohort involving 5 academic EDs in South Korea to study the CCHR, the NOC, and the NEXUS Head CT. Of the 696 meeting the CCHR eligibility requirements, the rule was 79.2% sensitive (95% CI 70.8% to 86.0%) and 41.3% specific (95% CI 37.3% to 45.5%) for detecting CIBI. Of the 657 patients meeting eligibility requirement for the NOC, the rule was 91.9% sensitive (95% CI 84.7% to 96.5%) and 22.4% specific (95% CI 19.0% to 26.1%).

Sensitivities reported were much lower than previous studies for CIBI, however specificity remained similar. The sensitivity for CIBI with the NEXUS Head CT was 88.7% (95% CI 85.8% to 91.2%) and specificity of 46.5% (95% CI 44.5% to 48.5%). The NEXUS Head CT sensitivity for neurosurgical intervention was 95.1% (95% CI 90.1% to 98%) and specificity was 41.4% (95% CI 39.5% to 43.2%). While the NEXUS Head CT was shown to reduce overall imaging in this trial, it also missed cases requiring neurosurgical intervention. Sensitivities for neurosurgical intervention were similar to previous reports at 100% for CCHR and NOC as all the patients with a need for neurosurgical intervention by CCHR and NOC were identified. This study suffered from selection bias as only 8.2% of the patients screened for enrollment were evaluated in the subsequent underpowered intersection cohort that included 588 patients.

Bouida et al,[53] in a Class III comparison study from Tunisia prospectively enrolled 1,582 patients in an observational cohort of patients with mild head injury comparing the CCHR and NOC. Sensitivity and specificity for need for neurosurgical intervention were 100% (95% CI 90% to 100%) and 60% (95% CI 44% to 76%) for the CCHR and 82% (95% CI 69% to 95%) and 26% (95% CI 24% to 28%) for the NOC. Sensitivity and specificity for clinically significant head CT findings were 95% (95% CI 92% to 98%) and 65% (95% CI 62% to 68%) for the CCHR and 86% (95% CI 81% to 91%) and 28% (95% CI 26% to 30%) for the NOC. While significant limitations applied to this study regarding loss of screened patients and data, proportion of patients imaged, the definition of clinically significant head CT findings, and follow-up, it did support the fact that decision tools may have performance patterns that change dependent upon the setting and population in which they are used. When adjusting for patients with GCS 15 in this trial, sensitivities for CCHR were 100% (95% CI 86% to 100%) and for NOC 96% (95% CI 80% to 100%); specificities were 58% (95% CI 55% to 61%) and 26% (95% CI 23% to 28%), respectively.

Certain subsets of head injured patients present additional concerns that may exclude them from established decisional aids such as those on anticoagulant or antiplatelet medications (excluding aspirin as a sole agent) and older patients. All 3 rules necessitate imaging in older patients regardless of other risk factors. Similarly, older patients (65 years and older in CCHR and NEXUS Head CT and 60 years and older in NOC) were considered high risk for CIBI, but data on age as an independent variable are limited.

Probst et al[54] (2020) in a Class III multi-center study enrolled a prospective cohort of 9,070 adult patients presenting with blunt head trauma who underwent CT imaging based on the clinical judgement of the treating physician (not by study protocol). Among this population, 1,323 (14.6%) were on either aspirin, clopidogrel, warfarin, or combination therapy and most (77.5%) had a GCS of 15. Compared to patients without any coagulopathy, the relative risk of significant intracranial injury was 1.29 (95% CI 0.88 to 1.87) for patients on aspirin alone, 0.75 (95% CI 0.24 to 2.30) for those on clopidogrel alone, and 1.88 (95% CI 1.28 to 2.75) for those only on warfarin. The relative risk of significant intracranial injury was 2.88 (95% CI 1.53 to 5.42) for patients receiving both aspirin and clopidogrel combination therapy. Additionally, the increased risk in patients receiving warfarin or those receiving both aspirin and clopidogrel persisted across most subgroup analysis. Given these results, clinicians would be prudent in having a lower threshold for imaging in these high-risk patients. Furthermore, while non-vitamin K antagonist oral anticoagulants (NOACs) have not been well studied in head trauma,[55,56] intuitively these patients are likely at higher risk for significant intracranial injury as well. Almost all studies reviewed included some patients on aspirin, but that particular antiplatelet agent by itself was not considered to be a factor in clinical decision-making.

As for intoxication, NOC included drug or alcohol intoxication as a higher risk feature. In the study,[48] this was defined as history from the patient or a witness and suggested by findings on exam like speech changes or odor on breath. Labs were only ordered by physician discretion. The derivation and validation studies for CCHR and NEXUS Head CT, while having included intoxicated patients, did not rely specifically on intoxication as a risk factor, but relied on GCS <15 or an abnormal level of alertness respectively as risk factors. In a Class III study, Easter et al[57] (2013) enrolled a prospective cohort of intoxicated adults with minor head injury presenting to an urban academic trauma center over a one-year period. A total of 283 patients were enrolled, with a GCS ≥14, the majority with a GCS 15 (80%). Clinically important injuries requiring admission or neurosurgical follow up were identified in 23 patients (8% [95% CI 5% to 12%]). While LOC and headache were associated with clinically important injury, the CCHR only had a sensitivity of 70% (95% CI 47% to 87%) and the NEXUS Head CT had a sensitivity of 83% (95% CI 61% to 95%). Given these results, while the presence of certain features such as headache may raise suspicion for significant injuries, the absence of high-risk criteria in CCHR and the NEXUS Head CT cannot alone eliminate the need for CT in intoxicated patients.

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520 **Table 2.** Comparison studies.

Study	Patients enrolled	Patients with CIBI	Sensitivity for CIBI (95% CI)	Specificity for CIBI (95% CI)
Stiell et al[50] Class II	1,822	97 (5.3%)	CCHR: 100% (96% to 100%) NOC: 100% (96% to 100%)	CCHR: 50.6% (48% to 53%) NOC: 12.7% (11% to 14%)
Smits et al[51] Class II *different definition of CIBI	3,181	243 (7.6%)	CCHR: 84.5% (78.1% to 89.3%) NOC: 97.7% (92.1% to 99.4%)	CCHR: 38.9% (35.6% to 42.3%) NOC: 5.5% (2.6% to 8.7%)
Easter et al[25] Class II Systematic review	23,079	1,639* 7.1% (95% CI 6.8% to 7.4%)	CCHR: 99% (78% to 100%) NOC: 99% (90% to 100%)	CCHR: 40% (34% to 46%) NOC: 13% (8.1% to 22%)
Mower et al[49] Class II	7,759 *comparison cohort, not overall NEXUS Head CT cohort	306 (3.94%)	CCHR: 98.4% (96.2% to 99.5%) NEXUS Head CT:97.7% (95.3% to 99.1%)	CCHR: 12.3% (11.6% to 13.1%) NEXUS Head CT:33.3% (32.3% to 34.4%)
Ro et al[52] Class III **data from original cohort outcomes compared with results of original articles **this study also has data for intersection cohort N=588 for all 3 tools	7,131	692 (9.7%)	CCHR: 79.2% (70.8% to 86.0%) NOC: 91.9% (84.7% to 96.5%) NEXUS Head CT:88.7% (85.8% to 91.2%)	CCHR: 41.3% (37.3% to 45.5%) NOC: 22.4% (19.0% to 26.1%) NEXUS Head CT: 46.5% (44.5% to 48.5%)
Bouida et al[53] Class III	1,582	218 (13.8%)	CCHR: 95% (92% to 98%) NOC: 86% (81% to 91%)	CCHR: 65% (62% to 68%) NOC: 28% (26% to 30%)

521 *CCHR*, Canadian Head CT Rule; *CIBI*, clinically important brain injury; *CT*, computed tomography; *NOC*, New
522 Orleans Criteria.
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Summary

Recognizing the growing emphasis of value-based care, clinical decision tools have gained attention as potential solutions for preserving patient safety while decreasing costs and using fewer resources. The CCHR and the NOC, along with the NEXUS Head CT, demonstrate excellent sensitivity regarding timely identification of significant intracranial injury. With well-demonstrated sensitivities of close to 100% (CCHR 95% CI 92% to 100%, NOC 95% CI 95% to 100%, NEXUS Head CT 95% CI 95.3% to 99.1%) for significant intracranial injury, the CCHR, NOC, and NEXUS Head CT can effectively aid in determining which patients do not need a head computed tomography.[47-49] The CCHR has higher specificity than the NOC; however, there are some limitations in specificity which may inhibit substantial reductions in CT imaging. While some studies have shown decreases in head CT imaging with application of a clinical decision tool,[58] others have shown no change or even an increase in use.[59,60] As with any clinical decision tool, those that address head injury must be applied to the population in which they were developed and validated. For example, applying these rules to higher volumes of lower risk populations could lead to increased specificity, while applying these rules to higher volumes of higher risk populations (less low risk) could lead to decreased specificity. Inclusion criteria for these rules restrict their use, and they are only valid when applied to patients who have had a LOC or amnesia and who are not on anticoagulants. While several other clinical decision tools exist for determining the need for head CT in minor head injury, none have been studied well enough to include in this policy. In conclusion, the NEXUS Head CT or NOC have similar sensitivities to the CCHR in providing decision support. However, as most studies show that the NEXUS Head CT and NOC have significantly lower specificity in adults (which may lead to more unnecessary testing), the CCHR is the more favored tool.

Future Research

Future research may help provide a broader application of clinical decision tools for mTBI or improved specificity or ideally, both. For example, the ability to apply a decision tool for a patient on an anticoagulant or antiplatelet therapy (exclusive of aspirin) or a patient who is intoxicated has some limitations, as previously noted. Perhaps there are some CT scans performed in these patient populations that are unnecessary. Serum biomarkers, such as S-100 calcium binding protein (S100B) or brain specific glial fibrillary acidic protein (GFAP) may add

additional information. The addition of biomarker information may then be combined with patient history and exam features or components of existing clinical decision tools, with the potential for increased specificity and decreased CT utilization. However, at this point, strong data on biomarker use with or without other decision tools is lacking and limited by availability of these tests. Future studies should investigate whether subsets of patients with coagulopathy, advanced age, NOAC or newer antiplatelet agent treatments, or intoxication may safely avoid imaging after minor blunt head trauma.

2. In the adult ED patient presenting with minor head injury, a normal baseline neurological examination, and taking an anticoagulant or anti-platelet medication, is discharge safe after a single head CT?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. Do not routinely perform repeat imaging in patients after a minor head injury who are taking anticoagulants or anti-platelet medication and are at their baseline neurological exam, provided the initial head CT showed no hemorrhage.

Do not routinely admit or observe patients after a minor head injury who are taking anticoagulants or antiplatelet medication who have an initial head CT without hemorrhage, and do not meet any other criteria for extended monitoring.

Level C recommendations. Provide instructions at discharge that include the symptoms of rare, delayed hemorrhage after a head injury (Consensus recommendation).

Consider outpatient referral for assessment of both fall risk and risk/benefit of anticoagulation therapy (Consensus recommendation).

Resources:

Discharge instructions and other materials for patients

- CDC Mild Traumatic Brain Injury and Concussion: Information for Adults: https://www.cdc.gov/traumaticbraininjury/pdf/TBI_Patient_Instructions-a.pdf
- CDC educational materials for adults with mTBI: https://www.cdc.gov/traumaticbraininjury/mtbi_guideline.html

Fall risk screening and assessment for providers and fall prevention materials for patients

- CDC Algorithm for Fall Risk Screening, Assessment & Intervention: https://www.cdc.gov/steadi/pdf/STEADI-Algorithm-508.pdf
- CDC fall prevention materials for patients: https://www.cdc.gov/steadi/patient.html

Potential Benefit of Implementing the Recommendations:

- A decrease in medical costs by avoiding unnecessary medical imaging or hospital observation or admission.
- Avoid inpatient health care associated complications by avoiding excessive duration of stay in the ED or hospital.
- A decrease in length of stay for patients that could go home early from the ED without repeat imaging or prolonged observation.

Potential Harm of Implementing the Recommendations:

- A missed case of posttraumatic intracranial hemorrhage that could have benefited from early intervention.

Key words/phrases for literature searches: brain concussion, brain injury, closed head injury, concussion, commotio cerebri, craniocerebral trauma, mild traumatic brain injury, minor head injury, mTBI, traumatic brain injury, anticoagulant, anticoagulant therapy, antiplatelet, antiplatelet medication, direct thrombin inhibitor, factor Xa inhibitor, apixaban, aspirin, betrixaban, clopidogrel, coumarin, dabigatran, dabigatran etexilate, dipyridamole, edoxaban, fondaprinux sodium, heparin, heparinoids, lepirudin, prasugrel, low molecular weight heparin, NOAC, non-vitamin K antagonist oral anticoagulant, rivaroxaban, ticlopidine, tinzaparin sodium, warfarin, brain computed tomography, CT scan, head computed tomography, head CT, x-ray computed tomography, and variations and combinations of the key words/phrases. Searches included January 2010 to search dates of January 16 and 22, and March 9 and 11, 2020.

Study Selection: Two hundred eighty-four articles were identified in the searches. Twenty-one articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, zero Class I studies, 1 Class II study, and 3 Class III studies were included for this critical question (Appendix E).

As the United States population continues to age, there is an increasing prevalence of anticoagulant and antiplatelet use. Most indications are for atrial fibrillation, cardiac valve replacement, and thromboembolic disease.[61] Older patients are also more prone to closed head injury, predominantly from falls.[62] The presence of these drugs, including NOACs, is associated with increased morbidity and mortality from intracranial hemorrhage. Antiplatelet agents are no safer in some series.[63] Therefore, the threshold for initial imaging after minor head trauma in patients on either anticoagulants or antiplatelet agents is very low due to the consequences of potentially missing an early hemorrhage.

The risk of spontaneous intracranial hemorrhage in association with anticoagulation is well described. Because of the higher incidence of significant intracranial injuries after blunt head trauma in patients on warfarin versus non-anticoagulated patients (3.9% versus 1.5%), the liberal use of neuroimaging on initial presentation is advocated.[54] Although the NOACs have lower incidence of intracranial hemorrhage (2.6% versus 10.2% for

vitamin K antagonists [VKAs]), it is still higher than in patients without any anticoagulation.[64] Although most agree on the need for an initial CT scan of the brain,[31] many clinicians are concerned of the possibility of delayed intracranial hemorrhage in patients on anticoagulants or antiplatelet agents, which has been cited to be as high as 6%.[65,66] European guidelines suggest that all patients on anticoagulants should undergo a period of routine observation after head injury, regardless of clinical presentation.[67] More recently, the value of observation has been questioned,[68] but does not address the need for repeat imaging. With the lack of national consensus guidelines regarding need for repeat imaging, there are a variety of approaches to these patients including serial neurological exam, observation, or hospital admission versus immediate discharge. Because of the risk of delayed hemorrhage, many physicians subject these patients to repeat brain imaging after a brief period (4 to 6 hours) of observation before discharge, even with a normal neurological exam.

Therefore, this clinical policy aims to clarify if a single CT scan is adequate (or acceptable) to exclude an intracranial hemorrhage after blunt head trauma. The target population were patients regularly taking anti-coagulants, which included warfarin and NOACs, or antiplatelet agents, which included clopidogrel and ticagrelor. The focus was on a safe ED discharge that avoided any subsequent clinically significant outcome due to intracranial hemorrhage, such as cranial surgery or death, after the initial visit related to the original injury. The main exclusion from this policy is the concomitant use of aspirin; there were not enough cases to make a recommendation for that particular antiplatelet agent.

The literature search and recommendations were limited to include only minor head injury. This included any blunt head trauma that could be severe enough to cause temporary LOC, or post-traumatic amnesia or disorientation, and have a minimum GCS of 14 on presentation to the ED.[47,69] We only included cases of isolated blunt head trauma in adults, at the minimum age 14 years or higher. Further review of the literature revealed a single Class II study, and 3 Class III studies that reported data pertinent to answering the critical question.

The only Class II study, Nishijima et al,[70] is a multicenter retrospective observational study of adults (≥18 years of age) with blunt traumatic injury. Although ultimately 1,064 patients were enrolled, most, 932 (87.6%), qualified as a patient with minor TBI who presented with a GCS of 15 and 752 (70.7%) had head trauma above the clavicles. Out of the 1,064 patients, 1,000 (94%) received a CT scan of the head, with 43 on concomitant aspirin. All 930 patients found to have normal initial CT scans were followed for 14 days, either as inpatients or

outpatients. Of the 687 patients on warfarin, 4 (0.6% [95% CI 0.2% to 1.5%]) had delayed intracranial hemorrhages with none requiring neurosurgical intervention, but 2 cases resulted in death. None of the 243 patients on clopidogrel had delayed intracranial brain hemorrhage (ICH), although 1 did die of unknown cause. Although a small number of patients were lost to follow up, the authors concluded that delayed ICH after a negative initial head CT scan is very rare in patients on warfarin or clopidogrel, and that these patients do not warrant admission for observation or immediate reversal of anticoagulation. Of note, only a small number of patients (43 total) in both groups (warfarin and clopidogrel) were on concomitant aspirin, but the drug did not seem to be associated with initial or delayed ICH.

The first Class III study, Menditto et al,[71] is a prospective case series of patients ≥14 years of age with minor head injury on warfarin who had an initial negative head CT scan. All were observed for ≈24 hours and had a repeat CT scan prior to discharge. Although 5 of 87 patients (6% [95% CI 1% to 11%]) had an intracranial injury on second CT scan, only 1 required neurosurgical intervention for a subdural hematoma. An additional 2 patients, who had a negative second CT scans at discharge, returned several days later with subdural hematomas. The authors concluded that they support the European Federation of Neurological Sciences recommendation of a 24-hour observation accompanied by a repeat CT scan for all anticoagulated patients with minor head injury. Based on this protocol, 1 patient in 87 will be identified that will require neurosurgical intervention. Limitations in this study included no blinded outcome assessment or adjudication of outcomes. Approximately 10% of qualifying subjects refused the second scan, but follow up showed they did well.

The second Class III study, Cipriano et al,[72] is a single-center prospective observational study that followed a cohort of adults on oral anticoagulant therapy who sustained a blunt head injury associated with an initial ED GCS 13 to 15 regardless of LOC. Out of the 206 patients, 121 were on VKAs, and 85 on NOACs. Since 183 of the 206 patients did not have an immediate intracranial hemorrhage (initial negative CT), and 5 patients were lost to follow-up, the final analysis group consisted of 178 patients. Of the 178 patients with normal CT head exams, dispositions included: immediate discharge without 24 hour observation (16), admission for medical reasons unrelated to the ICH (12), or observation for 24 hours prior to discharge (150). Out of the 150 patients who were observed, only 3 (2% [95% CI 0 to 4.2%]) had neurological deterioration, but they all had a second CT scan that was also negative for ICH. Ultimately, out of 178 patients followed for 30 days, only 3 (1.7%

[95% CI 0 to 3.6%]) had a positive CT scan for delayed ICH, with 1 death (0.6% [95% CI 0.5% to 1.7%]) and none with neurosurgical interventions. Although the study had some patients lost to follow up, the only delayed hemorrhage of clinical importance was 1 death in a patient that had already been admitted and experienced early neurological deterioration. The other caveat noted in this study is that most patients were observed prior to discharge.

The last class III study included in this analysis, Kaen et al,[73] is a prospective single-center study of patients with mild head injury, GCS 14 to 15, age >16 years, with or without LOC or posttraumatic amnesia on anticoagulant therapy (warfarin or heparin) who had an initial normal CT scan of the head. All were admitted and observed for 24 hours with serial neurological exams. At 20 to 24 hours post initial CT scan, a repeat was performed. Out of 137 patients, only 2 (1.4% [95% CI 1.0% to 1.8%]) showed hemorrhagic lesions on the repeat imaging. Neither patient required neurosurgical intervention nor adjustment of anticoagulation. Both patients were subsequently discharged without neurological sequelae. Of note, only 3 patients were on aspirin as well.

Taken together, all these studies suffer from limited patient numbers along with potential selection biases. Overall, there was a paucity of patients on aspirin, with or without concomitant anticoagulants, in these studies, as well as limited numbers of patients on NOACs. Regardless, collectively these studies all support the notion that delayed intracranial hemorrhage after blunt head trauma in neurologically intact patients on anticoagulant or antiplatelet therapy is rare (Table 3). Even if delayed intracranial hemorrhage does occur, it tends not to be clinically significant and not necessitate neurosurgical intervention. The data suggest that patients on anticoagulants, or antiplatelet agents, with a normal initial head CT after blunt trauma, and who are neurologically intact, can be safely discharged. Most studies included a brief observation period, which is fortunate for research follow up, but ultimately unnecessary due to lack of ICHs or neurological deterioration during that additional period. Due to the potential for up to approximately 5% of these patients to develop delayed intracranial hemorrhage, clear discharge instructions with return precautions are warranted. Most studies did not state if patients had their anticoagulant or antiplatelet medication withheld for the first few hours or days after the injury, which would require weighing the chance of repeat trauma (fall) or lack of good social support for home observation. However, with the low incidence of delayed ICH, there is not a strong argument for withholding these medications if the patients are not suspected to be supratherapeutic.

TABLE 3. Comparison of incidence of delayed ICH after initial negative CT scan in all four studies.

STUDY	Blood Thinner	N	Delayed ICH (NS intervention)	% Incidence (95% CI)
Nishijima et al[70]	Warfarin	687	4 (0)	0.6% (0.2% to1.5%)
	Clopidogrel	243	0 (0)	0% (0 to 1.5%)
Kaen et al[73]	Warfarin	137	2 (0)	1.4% (0.4% to 5.2%)
Menditto et al[71]	Warfarin	87	5 (1)	5.6% (2.5% to 12.8%)
Cipriano et al[72]	Warfarin	99	1 (0)	1.0% (0.2% to 5.5%)
	NOACs	79	2 (0)	2.5% (0.7% to 8.8%)

Summary

Anticoagulants (VKA and NOACs), and to some extent antiplatelet agents, are associated with a higher risk of intracranial hemorrhage after mild head trauma. Initial neuroimaging should be sufficient to exclude any clinically significant injuries in patients who appear otherwise neurologically intact at baseline. Based on the lack of increased delayed ICH, patients who are neurologically intact can be safely discharged without need for repeat imaging or observation admission specifically for head injury. The only caveat is that all patients, especially vulnerable older persons, should have someone who can follow discharge care instructions and/or help provide a safe environment during their recovery.[74-76]

Future Research

Future research should focus on predictive factors for higher risk of decompensation, along with the use of pre-injury aspirin, for the few patients that do sustain delayed intracranial hemorrhage after minor head trauma. Also, based on the low incidence of ICH on initial imaging, research could focus on trying to reduce unnecessary CT scanning on initial presentation for these patients. Quantification of the economic benefit of reduced repeat imaging and observation times is needed. Finally, the role of shared decision making, especially in vulnerable older adults, needs to be evaluated.

3. In the adult ED patient diagnosed with mild traumatic brain injury or concussion, are there clinical decision tools or factors to identify patients requiring follow-up care for post-concussive syndrome or to identify patients with delayed sequelae after ED discharge?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Consider referral for potential higher risk patients with post-concussive syndrome (PCS) with the following: female sex; previous pre-concussive psychiatric history; Glasgow Coma Scale score <15; etiology of assault, acute intoxication; loss of consciousness; and pre-injury psychological history such as anxiety/depression.

Do not utilize current diagnostic tools (including biomarkers) to reliably predict which patients are at risk for PCS.

Provide concussion specific discharge instructions and selected outpatient referral of patients at high risk for prolonged PCS (Consensus recommendation).

Resources:

Discharge instructions and other materials for patients

- CDC Mild Traumatic Brain Injury and Concussion: Information for Adults https://www.cdc.gov/traumaticbraininjury/pdf/TBI_Patient_Instructions-a.pdf
- CDC educational materials for adults with mTBI: https://www.cdc.gov/traumaticbraininjury/mtbi_guideline.html

Potential Benefit of Implementing the Recommendations:

- The ability to predict and screen for patients at risk for PCS allows for early recognition and potential interventions such as referral to multidisciplinary concussion programs or modifications in post visit behaviors.

Potential Harm of Implementing the Recommendations:

- Missing "clinically important findings" or associated injuries could lead to increased morbidity and mortality if a utilized tool is poorly proven.
- Misapplication of a tool for patients inappropriately identified as high-risk individuals could result in excessive patient concern, anxiety, or unneeded interventions adding to costs.

Key words/phrases for literature searches: brain concussion, brain injury, closed head injury, coomotio cerebri, concussion, head injury, head trauma, mild traumatic brain injury, mTBI, minor head injury, traumatic brain injury, clinical criteria, clinical decision, clinical decision instrument, clinical decision rule, clinical decision tool, clinical prediction instrument, clinical prediction rule, clinical prediction tool, decision support instrument, decision support techniques, cognitive aid, screening aid, screening tool, screening marker, screening criteria, biomarkers, post-concussive syndrome, delayed sequelae, emergency care, emergency department, and variations and combinations of the key words/phrases. Searches included January 2010 to search dates of January 17 and 22, and March 9 and 11, 2020.

Study Selection: Three hundred and sixty-seven articles were identified in the searches. Forty-four articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, zero Class I studies, zero Class II studies, and 9 Class III studies were included for this critical question (Appendix E).

Several studies examined multiple modalities to predict the likelihood of PCS, symptoms of PCS, and/or delayed sequelae after ED discharge. There would be a direct clinical benefit in the development of a single parsimonious bedside tool to risk stratify individuals in the ED for referral to neuropsychiatric clinical follow-up or the ability to predict potentially protracted symptoms and sequelae. Following mTBI, there is an ill-defined subset of patients whose prolonged course post-injury results in increased morbidity associated with decreased function at home: while driving, at work, and on the athletic field in sporting activities. However, studies of prolonged or long-term follow-up are limited and resolution of time courses for PCS have varying agreement.[77,78] Each compiled and assessed study attempts to delineate this subgroup, working with variable definitions and mixed tools, for the assessment and stratification of at-risk, post-discharge, mTBI patients presenting to the ED.

The 9 included studies are all Class III and vary in their definitions of mTBI, making a singular generalizable recommendation on this patient group difficult. Included studies differ in their decision tools, the variable nature and often unclear baseline neurocognitive status prior to injury, inclusion criteria, duration of follow-up, and outcome definitions. The patient populations, as defined across the range of articles, are heterogeneous along with variable study methodologies. A recurrent challenge in this research is in the definitions related to PCS. Criteria standards vary for PCS, and therefore serve to alter adhered to definitions and nomenclature across various studies. In addition, total symptom duration for the PCS is not understood well, resulting in variable periods of follow-up for all the included studies.

Of the included studies, many utilized a battery of tests conducted in the ED with an objective follow-up assessment tool in order to predict risk of PCS based upon ED patient characteristics and examination variables. Subbian et al,[79] conducted a Class III prospective observational study of 66 ED patients with blunt head trauma and a clinical diagnosis of isolated mTBI made by the treating physician. In the ED, a battery of robotic assisted tests was performed assessing proprioceptive, visuomotor, visuospatial, and executive functions upon inception. Three weeks post-injury patients were contacted to complete the Rivermead Post-Concussion Questionnaire (RPQ) to assess for the presence of symptoms consistent with PCS. The RPQ consists of 16 symptoms associated with concussion that are assessed on a severity scale from 0 to 4 based upon subjective symptoms at the time of administration.[80] Of the 66 enrolled, 42 completed both the initial assessment and the subsequent follow-up questionnaire and ultimately 40 were included in the final analysis. The area under the curve (AUC) for the entire

battery of tests was 0.72 (95% CI 0.54 to 0.90) and the AUC for visuomotor and proprioceptive performance was 0.80 (95% CI 0.65 to 0.95) and 0.71 (95% CI 0.53 to 0.89), respectively. Although this study was prospective with sound methodology, this was a labor-intensive single-centered study with a small number of patients enrolled and followed through to completion. The assessment battery required careful training and assessment with the use of a robotic-assisted device to ensure the initial and follow-up evaluations were performed adequately and in accordance with study design. This would be challenging in standard ED settings to perform routinely as most EDs are not equipped with such a testing apparatus.

Sheedy et al,[81] a Class III prospective case series utilizing a convenience sample from a single hospital in Australia, applied a similar methodology as in the article by Subbian et al.[79] Enrolled patients were assessed by a battery of tests at inception including neuropsychological functioning, acute pain scores, and postural stability. In the subsequent telephone follow-up at 3-months post-injury, patients were assessed with the RPQ. Patients with neuropsychological defects, acute pain, or postural instability at the time of ED assessment were statistically associated with continued post-concussive symptoms at 3 months. Utilizing a regression formula, a simple measure within the ED—immediate and delayed recall of 5 words and a visual analogue scale score of acute headache—resulted in 80% sensitivity and 76% specificity for the prediction of post-concussive symptoms at 3 months. The study was small, single centered, and based primarily on a convenience sample, so it is therefore difficult to secondarily generalize to other ED populations.

Multiple other graded and included studies contained methodology that had been datamined from reassessments of larger studies that were not initially designed to answer the primary question of concern for the ED provider. In a Class III study by Brooker et al,[82] data was utilized from a larger cohort to perform an observational study of mTBI in the ED utilizing the SHEFfield Brain Injury After Trauma study to assess long term disability utilizing the RPQ and the Rivermead Post-Injury Follow-up Questionnaire. Of the 1,322 patients initially approached, 575 mTBI patients were analyzed and enrolled in the multivariate analysis. Female gender, previous psychiatric history, GCS <15, etiology of assault, and alcohol intoxication were associated with prolonged symptoms and worse outcomes in recovery.

A Class III trial by Kraus et al[83] performed a secondary analysis of a larger cohort utilizing the RPQ and indicators of health services used and social disruptions at 3- and 6-months post-discharge of mTBI patients

versus those without injury. RPQ symptoms, health service utilization, and 5 indicators of social disruption or function were found to be higher in the mTBI group, indicating significant morbidity in this cohort. These problems may persist for at least 6 months and this study shows the need for not only continued medical care, but also the potential need for social assistance with things such as driving support, employment issues, and financial assistance during recovery.

In a Class III secondary analysis of a larger trial, Ponsford et al[84] (2019) assessed 343 individuals with mTBI out of a larger cohort of the NET trial involving 31 Australian EDs. Each enrolled participant completed the RPQ, the Anxiety scale of the Hospital Anxiety and Depression Scale (HADS), and the Quality of Life (QOL)—Short Form. Three or more post-concussive symptoms were reported in 18.7% of the participants, most frequently fatigue (17.2%) and forgetfulness (14.6%). Predictors of post-concussive symptoms included the following: pre-injury psychological issues, LOC, and having no recall of receiving information regarding brain injury from the ED.

Prior to this, in a Class III 2012 study utilizing a secondary analysis of a larger study, Ponsford et al[85] (2012) compared 123 patients with mTBI versus 100 trauma controls recruited and assessed in the ED and followed-up at 1 week and 3 months post-injury. Multiple outcome measures were utilized which included a self-reported PCS measured by the ImPACT Post-Concussion Symptom Inventory (22 post concussive symptoms) with a severity scale, a cognitive battery including 5 test modules (attention, verbal memory, visual memory, processing speed, reaction time); pre- and post-injury SF-36; the Mini-International Neuropsychiatric Interview (MINI); a pain Visual Analogue Scale (VAS); Hospital Anxiety and Depression Scale (HADS); PTSD Checklist Specific (PCLS); Revised Social Readjustment Rating Scale (RSRRS); and questions regarding narcotic use and litigation. Mild TBI predicted PCS at 1-week post-injury with the following: female gender, premorbid psychiatric history, and increased HADS anxiety, whereas at 3 months, anxiety and age were better predictors of PCS in mTBI. Potentially targeting patients with notable anxiety after mTBI or a history of anxiety might be helpful. Prospective interventions with outcomes assessing this and other factors would be of much interest.

The 2017 Class III study by Scheenen et al[86] performed a subgroup analysis of a larger prospective cohort study. The 820 patients with mTBI were evaluated to compare patient characteristics and associations in those with persistent post-concussive symptoms at 2 weeks post-ED discharge. It was found that female gender and

psychological factors such as coping styles, depression, anxiety, and PTSD symptoms best predicted the identification of patients at risk for persistent symptoms.

In an alternative approach to this question, Su et al[87] conducted a Class III retrospective cohort study in patients with isolated mTBI from 4 institutions in China assessing the plasma biomarker high-sensitivity C-reactive protein (hs-CRP) at baseline and 1,2,3 months follow-up. The endpoints included persistent PCS, persistent psychological problems (depression and anxiety), and persistent physiological problems (frequent headaches, nausea, insomnia, dizziness, and fatigue [at least one/week]), and persistent cognitive impairments. Elevated baseline hs-CRP was associated with a statistically significant increase in persistent PCS, (odds ratio (OR) 2.72; 95% CI 1.61 to 4.59), persistent psychological problems (OR 1.54; 95% CI 1.06 to 2.22), and persistent cognitive impairment (OR 1.69; 95% CI 1.14 to 2.51). However, elevated hs-CRP levels were not associated with persistent physiological problems (OR 1.33; 95% CI 0.91 to 1.96). The study had a small loss to follow-up (<10%), but it is only based upon 213 patients and has yet to be reproduced on a larger scale in order to be better externally validated.

The only imaging study included in this review was a Class III prospective cohort study by Lange et al[88] performed at a Level 1 Trauma Center in Canada. The study evaluated 108 ED patients recruited following mTBI or orthopedic injuries without brain injury (72 mTBI and 36 controls) and determined the ability of white matter changes as discovered on diffusion tensor imaging (DTI) magnetic resonance imaging (MRI) to predict PCS. Ultimately the study found no ability for the novel imaging modality to discern PCS in patients from those without.

Summary

Post-concussion syndrome is a poorly understood clinical entity that requires increased medical and social resources and is associated with significant morbidity, particularly concerning neurocognitive functioning. The ability to predict at risk individuals in the ED after an inciting mTBI may have implications for post-discharge interventions. These might include, but are not limited to, post-discharge precautions regarding limitation in physical and cognitive activity, avoidance of activities that exacerbate symptoms, and referral to multidisciplinary teams for early interventions. However, most of these interventions still have unknown efficacy in reducing any

potential negative impact on quality of life. In this review, 9 articles with Class III evidence were included assessing the predictive ability of ED screening modalities as well as diagnostic entities. Multiple studies assessed a battery of cognitive testing performed in the ED particularly concerning pain, visuospatial and visuomotor functioning at onset, and found an association between the performance in these tests and subsequent development of PCS. These studies all suffer from the same methodological limitations as secondary analyses of larger cohorts and demonstrate only interesting associations without any ability to discern causation. In addition, the studies demonstrate an association between psychiatric comorbidity, particularly defined as anxiety and depression, and the development of persistent PCS. Formal diagnostic testing has shown limited promise with hs-CRP, although this was a small study and DTI MRI was not useful.

Future Research

Future research should include prospective randomized or observational cohort trials of ED patients presenting with and without mTBI to delineate the risk factors, duration, demographics, patient-oriented outcomes like quality of life, and natural progression of PCS among a diverse cohort of patients that present to an ED. In addition, it would be beneficial to determine the contribution of health disparities (eg, race, sex, socioeconomic factors) on the differences in the development and mitigation of PCS. A fruitful venture for research will include the evaluation of early neurocognitive interventions of patients at high risk for persistent PCS to determine if early recognition and treatment reduces morbidity along with a determination of which, if any, of the appropriate neurocognitive battery of tests are expedient, reliable, accurate, and feasible to the ED clinician evaluating mTBI and screening for PCS. The role of newer imaging modalities such as trans-cranial ultrasound, positron emission tomography (PET), or alternative MRI protocols must be investigated to determine if there are imaging predictors of PCS. The role of biomarkers in the identification of patients with PCS or their possible roles in assessing disease progression or healing must also be better investigated. Finally, additional studies are needed to better determine the necessity and impact of post discharge precautions, the assessment and treatment of physical and cognitive symptoms with neurocognitive interventions, and the assessment of other efforts to decrease the incidence and symptomatology of PCS to improve long term outcomes, especially among high-risk groups.

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Appendix A. Definitions.

Adult: For the prior policy,[31] the term adult was used. However, a few studies with minor head injury in adults included some older adolescent aged patients, typically age 16 years and older. For this policy and for continuity with the previous policy, the term adult will refer to any older adolescent or young adult through the ages of older adulthood.

Anti-platelet: Any anti-platelet medication including the following examples: aspirin, clopidogrel, prasugrel, dipyridamole, ticlopidine.

Anticoagulant: Any anticoagulant medication including the following: coumarins (warfarin), heparins, or non-vitamin K antagonist oral anticoagulants (NOACs) such as direct thrombin inhibitors (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban, edoxaban, or betrixaban).

Baseline neurological exam: A normal baseline neurological status for the specific patient. For example, if a patient has had a prior CVA and no acute neurological exam findings are noted during evaluation, then this would be considered the patient's baseline.

Clinically important findings: "Clinically significant" abnormalities on CT requiring procedural intervention or admission, presence of neurological deterioration, intubation for the head injury, or death due to head injury.

Clinical decision tools: Any decision rules, tools, instruments, or aids, but may also include other assessment tools including combinations of cognitive aids, decision support instruments, screening aids, or biomarkers

Head CT: Non-contrast brain computed tomography.

Delayed traumatic intracranial hemorrhage: Traumatic intracranial hemorrhage on brain CT within 2 weeks after initial normal CT scan and without repeated head trauma history.[70]

Post-concussive syndrome (PCS): Any prolonged or delayed sequelae with physical, cognitive, or emotional symptoms associated with mTBI that last beyond the early period post injury and typically last weeks to months.[89]

Minor head injury and mTBI:
Patients with blunt head injury with GCS 14 or 15* (and improvement to GCS 15 at 2 hours post injury if GCS 14) with or without a history of the following: LOC, amnesia, or disorientation.
There is no universally accepted definition. This policy, in staying consistent with the ACEP Clinical Policy in 2008, will address patients with a GCS 14 or 15 since some experts and authors note a higher or moderate risk in patients with a GCS of 13.[31]

*This was a joint policy involving ACEP and CDC. Subsequent reports from the CDC define GCS 13-15 as mTBI. VA/DoD has now removed GCS in their definition of mTBI.[43]

Examples of other various definitions include:

- History of LOC, amnesia, or disorientation and GCS 13 to 15.[47]
  or
- History of LOC, normal findings on brief neurological exam (normal CNs, normal strength and sensation in arms and legs), and GCS 15 on arrival [LOC defined as reported by witness or patient or patient could not remember event (amnesia)].[48]
  or
- Any blunt head injury regardless of LOC or amnesia.[70]
  or

- Head injury (any trauma to the head, other than superficial injuries to the face) and presenting GCS score of 14 to 15 regardless of LOC.[71]

Appendix B. Literature classification schema.*

Design/ Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series	Case series	Case series

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

Appendix C. Approach to downgrading strength of evidence.

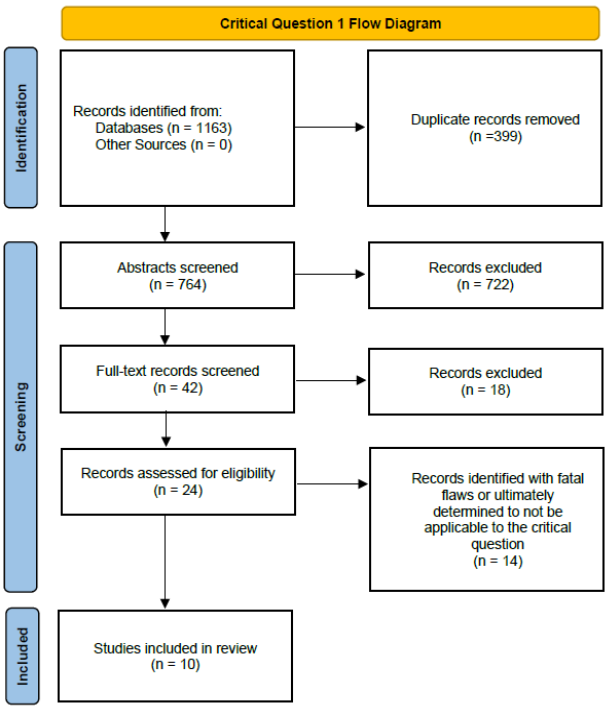
	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

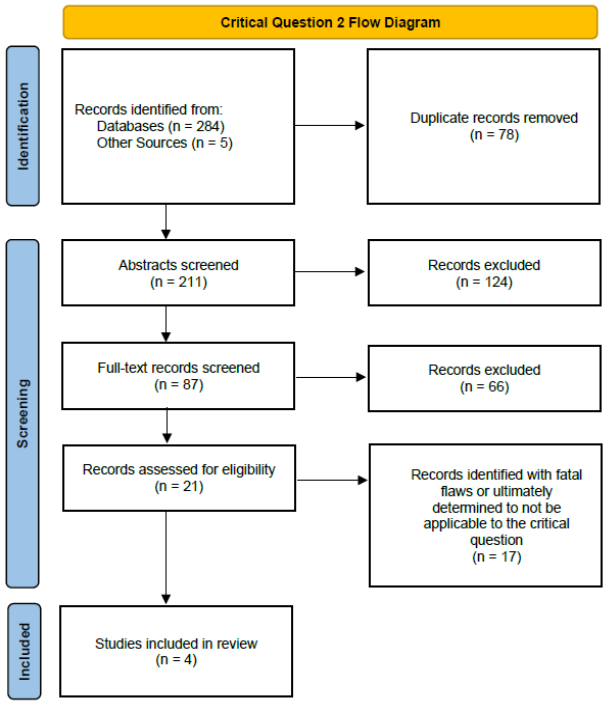
Appendix D. Likelihood ratios and number needed to treat.*

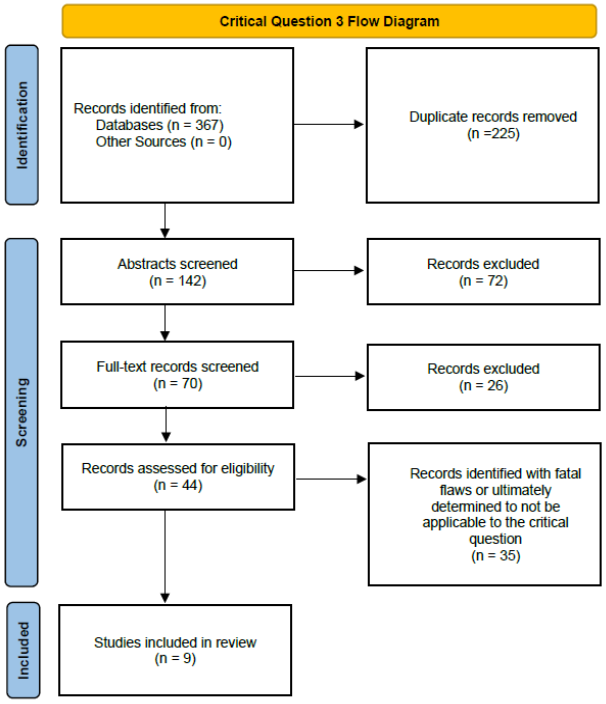
LR (+)	LR (–)	
1.0	1.0	Does not change pretest probability
1–5	0.5–1	Minimally changes pretest probability
10	0.1	May be diagnostic if the result is concordant with pretest probability
20	0.05	Usually diagnostic
100	0.01	Almost always diagnostic even in the setting of low or high pretest probability

LR, likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reduction×100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).

Appendix E. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagrams.[46]







Checklist to Assess for and Manage Mild Traumatic Brain Injury (mTBI) Concussion

For Emergency Department Providers Treating Patients 18 Years and Older

Assess.

- ☑ Conduct a physical examination to identify findings that may:
  - Suggest a more severe traumatic brain injury (e.g., hemotympanum)
  - Impact mTBI management (e.g., baseline deficits, oculomotor dysfunction)
- ☑ Assess symptoms using validated scales. Consider cognitive and balance testing.
- ☑ Do not image routinely (including CT & MRI). Use clinical decision rules to determine need.
- ☑ Do not use diagnostic tools (including biomarkers) to predict post-concussive syndrome.
- ☑ **For patients on anticoagulation or antiplatelet therapy (except for aspirin):**
  - **Highly consider imaging**
  - **Do not use clinical decision rules to exclude the need for head CT**
  - **Do not routinely repeat imaging if CT showed no hemorrhage at baseline**
  - **Do not routinely admit to hospital if CT is negative and no other medical criteria indicating admission are present**

Examples of validated scales:

- Standardized Assessment of Concussion
- Post-Concussion Symptom Scale
- Acute Concussion Evaluation
- Sport Concussion Assessment Tool

Examples of validated decision rules:

- Canadian CT Head Rule
- New Orleans/Charity Head Trauma/Injury Rule
- NEXUS

Educate.

- ☑ Provide discharge information about:
  - Rare symptoms of delayed hemorrhage
  - Typical recovery course
  - Gradual return to activity that does not worsen symptoms
- ☑ Offer clear instructions (preferably verbal and written) on return to activity customized to the patient's symptoms.

CDC patient discharge instructions:
www.cdc.gov/TraumaticBrainInjury

Example return-to-activity instructions:

After 2-3 days of rest, begin light activity and then gradually reintroduce regular non-sports-related activities that do not cause symptoms (such as headaches) to reappear or get worse.

Refer.

- ☑ Instruct patient to follow-up with their regular healthcare provider within a few days post-injury.
- ☑ Consider referral to outpatient care for patient at high risk for post-concussive syndrome.
- ☑ **For patients on anticoagulation or antiplatelet therapy (except for aspirin) consider outpatient referral to assess:**
  - **Fall risk**
  - **Risks and benefits of anticoagulation therapy**

Female patients are more likely to experience post-concussive symptoms. Risk factors for post-concussive syndrome also include:

- Psychiatric history
- GCS<15
- Etiology of assault
- Alcohol intoxication
- Loss of consciousness following injury
- Pre-injury anxiety or depression

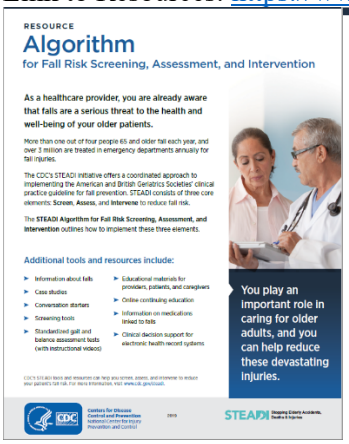
CDC older adult fall prevention tools:
www.cdc.gov/STEADI

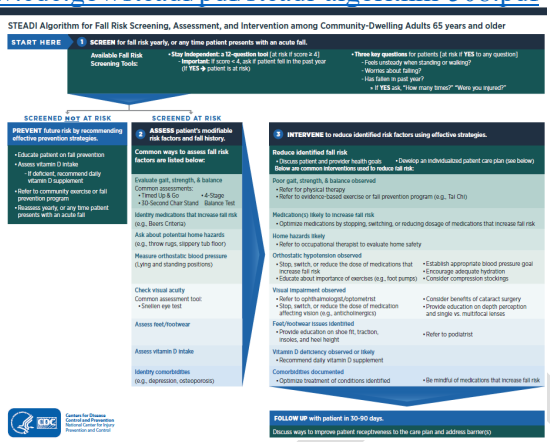
The full list of clinical recommendations and education tools related to the American College of Emergency Physicians mTBI Guideline is available at www.cdc.gov/TraumaticBrainInjury.

Appendix G. CDC educational tools and resources. (continued)

Algorithm for Fall Risk Screening, Assessment and Intervention

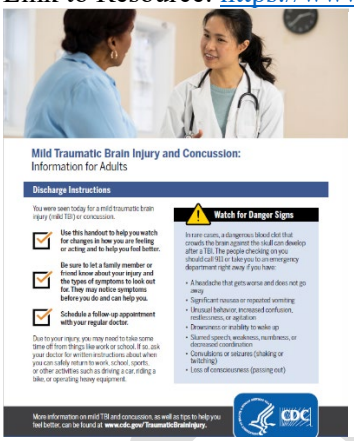
Link to Resources: https://www.cdc.gov/steadi/pdf/steadi-algorithm-508.pdf

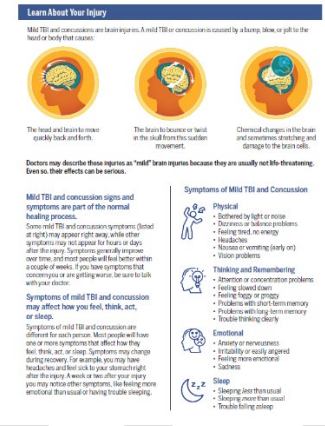


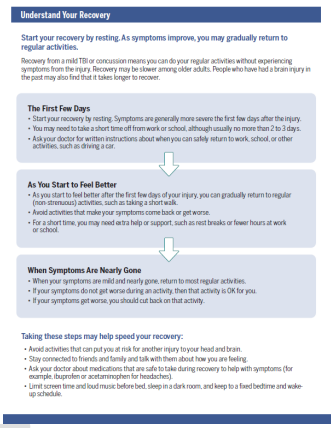


Mild Traumatic Brain Injury and Concussion: Information for Adults

Link to Resource: https://www.cdc.gov/traumaticbraininjury/pdf/tbi_patient_instructions-a.pdf







Stay Independent Brochure

Link to Resources: https://www.cdc.gov/steadi/pdf/STEADI-Brochure-StayIndependent-508.pdf

Check Your Risk for Falling

Circle "Yes" or "No" for each statement below			Why it matters
Yes (2)	No (0)	I have fallen in the past year.	People who have fallen once are likely to fall again.
Yes (2)	No (0)	I use or have been advised to use a cane or walker to get around safely.	People who have been advised to use a cane or walker may already be more likely to fall.
Yes (1)	No (0)	Sometimes I feel unsteady when I am walking.	Unsteadiness or needing support while walking are signs of poor balance.
Yes (1)	No (0)	I steady myself by holding onto furniture when walking at home.	This is also a sign of poor balance.
Yes (1)	No (0)	I am worried about falling.	People who are worried about falling are more likely to fall.
Yes (1)	No (0)	I need to push with my hands to stand up from a chair.	This is a sign of weak leg muscles, a major reason for falling.
Yes (1)	No (0)	I have some trouble stepping up onto a curb.	This is also a sign of weak leg muscles.
Yes (1)	No (0)	I often have to rush to the toilet.	Rushing to the bathroom, especially at night, increases your chance of falling.
Yes (1)	No (0)	I have lost some feeling in my feet.	Numbness in your feet can cause stumbles and lead to falls.
Yes (1)	No (0)	I take medicine that sometimes makes me feel light-headed or more tired than usual.	Side effects from medicines can sometimes increase your chance of falling.
Yes (1)	No (0)	I take medicine to help me sleep or improve my mood.	These medicines can sometimes increase your chance of falling.
Yes (1)	No (0)	I often feel sad or depressed.	Symptoms of depression, such as not feeling well or feeling slowed down, are linked to falls.
Total		Add up the number of points for each "yes" answer. If you scored 4 points or more, you may be at risk for falling.	

Appendix G. CDC educational tools and resources. (continued)

What You can do to Prevent Falls

https://www.cdc.gov/steadi/pdf/STEADI-Brochure-WhatYouCanDo-508.pdf

Evidentiary Table.

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Stiell et al[47] (2001)	II for Q1	Prospective cohort in 10 Canadian hospitals (community and academic) from 1996 to1999	Patients ≥16 y with mTBI and GCS 13 to 15 had predictor variable applied and then univariate analyses and then logistic regression to develop model with outcome of need for neurologic intervention (secondary outcome of clinically important brain injury)	3,121 patients 8% had clinically important brain injury; and 44 (1%) required neurological intervention; the high-risk factors were 100% sensitive (95% CI 92% to 100%) for predicting need for neurological intervention, and would require only 32% of patients to undergo CT; the medium-risk factors were 98.4% sensitive (95% CI 96% to 99%) and 49.6% specific for predicting clinically important brain injury, and would require only 54% of patients to undergo CT	Derivation study only with internal validation, but not yet externally validated (at the point when this article was published); otherwise, very strong methods, inclusive of robust follow-up
Haydel et al[48] (2000)	III for Q1	Prospective cohort	Patients >3 y with minor head injury who received CT; recursive partitioning applied to derive high risk criteria in phase 1 then applied to second phase of patients looking for positive CT	520 patients in the first phase, 36 (6.9%) had positive scans; all patients with positive CT scans had 1 or more of 7 findings; among the 909 patients in the second phase, 57 (6.3 %) had positive scans; in this group of patients, the sensitivity of the 7 findings combined was 100 % (95 % CI 95% to 100%); all patients with positive CT scans had at least 1 of the findings	Essentially an internal validation as the validation cohort, albeit separate from the derivation cohort, but validation occurred at same clinical site; also, minor concern about spectrum/selection as patients without LOC were not included; possible work-up bias

Evidentiary Table (continued). 1384

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Mower et al[49] (2017)	II for Q1	Prospective observation study from 2006 to 2015 in 4 academic EDs	All patients with mTBI that received head computed tomography; NEXUS criteria applied; need for neurosurgical intervention	12,696 patients with assessment in 11,817 with NEXUS Head CT decision instrument correctly assigned high risk status to 420 of the 420 patients requiring neurosurgical intervention yielding a sensitivity 100% (95% CI 99.1% to 100%); the instrument correctly assigned low risk status to 2,823 of 11,350 patients, specificity of 24.9% (95% CI 24.1% to 25.7%)	
Stiell et al[50] (2005)	II for Q1	Prospective cohort in 9 Canadian community and academic EDs from 2000 to 2002	Patients ≥16 y with mTBI had CCHR and NOC applied with outcome of neurosurgical intervention and clinically important brain injury	1,822 patients; 8 (0.4%) required neurosurgical intervention and 97 (5.3%) had clinically important brain injury; the NOC and the CCHR both had 100% sensitivity, but the CCHR was more specific (76.3% versus 12.1%, *P*<.001) for predicting need for neurosurgical intervention; for clinically important brain injury, the CCHR and the NOC had similar sensitivity (100% vs 100%; 95% CI 96% to 100%) but the CCHR was more specific (50.6% vs 12.7%, *P*<.001), and would result in lower CT rates (52.1% vs 88.0%, *P*<.001	The CCHR was applied in some of the EDs for which it was derived; small proportion (~10%) of lost to follow-up for outcome proxy assessment

Evidentiary Table (continued). 1385

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Smits et al[51] (2005)	II for Q1	Prospective observational study in 4 academic EDs in the Netherland from 2002 to 2004	Patients ≥16 y with mTBI, head computed tomography and GCS 13 to 15 with at least 1 risk factor; used variables from prior decision instruments and performed multivariable logistic regression analysis; outcome of any traumatic intracranial finding	3,181 patients, 243 (77.9%) had intracranial traumatic CT findings and 17 (0.5%) underwent neurosurgical intervention; a detailed prediction rule was developed from which a simple rule was derived; sensitivity of both rules was 100% for neurosurgical interventions, with an associated specificity of 23% to 30%; for intracranial traumatic CT findings, sensitivity and specificity were 94% to 96% and 25% to 32%, respectively	Outcome assessments were not blinded or independent; no chart review methods; all patients were evaluated in the ED by neurologist
Easter et al[25] (2015)	II for Q1	Systematic review	The MEDLINE database (1966 to August 2015) and the Cochrane Library were searched to identify English-language studies that evaluated the identification of traumatic brain injuries using history and physical examination; patients ≥18 y and older, GCS 13 to 15	2,760 studies identified, 14 included with 23,079 patients; when the CCHR was applied to patients with GCS scores of 13 to 15 and LOC, amnesia, or disorientation, the rule identified patients presenting with minor head trauma at low risk of severe intracranial injury, LR=0.04; (95% CI 0 to 0.65); using the summary prevalence of 7.1%, the absence of all the features on the CCHR lowers the probability of a severe intracranial injury to 0.31% (95% CI 0% to 4.7%); the NOC also accurately identified patients at lower risk of intracranial injury, LR=0.08 (95% CI 0.01 to 0.84); using the summary prevalence of 7.1%, the absence of any of the NOC lowers the probability of a severe intracranial injury to 0.61%	Not adjudicated

Evidentiary Table (continued). 1386

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Ro et al[52] (2011)	III for Q1	Prospective observational cohort from 2008 to 2009 at 5 academic EDs in South Korea	Patient's entry criteria were exactly the same as defined by each individual decision instrument (CCHR, NOC, NEXUS) and each rule was applied to consecutive patients with the outcome traumatic finding identified on CT scan that required hospital admission and neurosurgical follow-up	7,131 patients were prospectively enrolled, including 692 (9.7%) with clinical traumatic brain injury; among the enrolled population, patients eligible for CCHR, NOC, and NEXUS-II totaled 696,677, and 2,951, respectively; the sensitivity and specificity for clinically important brain injury were as follows: CCHR, 112 of 144 (79.2%, 95% CI 70.8% to 86.0%) and 228 of 552 (41.3%, 95% CI 37.3% to 45.5%); NOC, 91 of 99 (91.9%, 95% CI 84.7% to 96.5%) and 125 of 558 (22.4%, 95% CI 19.0% to 26.1%); and NEXUS-II, 511 of 576 (88.7%, 95% CI 85.8% to 91.2%) and 1,104 of 2,375 (46.5%, 95% CI 44.5% to 48.5%); the sensitivity and specificity for neurosurgical intervention were as follows: CCHR, 100% (95% CI 59.0% to 100.0%) and 38.3% (95% CI 34.5% to 41.9%); NOC, 100% (95% CI 54.1% to 100.0%) and 20.4% (95% CI 17.4% to 23.7%); and NEXUS-II, 95.1% (95% CI 90.1% to 98.0%) and 41.4% (95%CI 39.5% to 43.2%); among the enrolled population, intersection patients of CCHR, NOC, and NEXUS-II totaled 588; the sensitivity and specificity for clinically important brain injury were as follows: CCHR, 73 of 98 (74.5%, 95% CI 64.7% to 82.8%) and 201 of 490 (41.0%, 95% CI 36.6% to 45.5%); NOC, 89 of 98 (90.8%, 95% CI 83.3% to 95.7%) and 112 of 490 (22.9%, 95% CI 19.2% to 26.8%); and NEXUS-II, 82 of 98 (83.7%, 95% CI 74.8% to 90.4%) and 172 of 490 (35.1%, 95% CI 30.9% to 39.5%)	Selection/spectrum bias as <10% of all patients screened were included in analysis

Evidentiary Table (continued). 1387

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Bouida et al[53] (2013)	III for Q1	Observational cohort from 2008 to 2011 in teaching and non-teaching EDs in Tunisia	Patients with mild head injury age >10 y defined by blunt head trauma, GCS 13 to 15 and 1 other risk factor, primary outcome was need for neurosurgical intervention defined as either death or craniotomy or need of intubation within 15 days of the traumatic event; secondary outcome was the presence of traumatic lesions on head CT scan	1,582 patients enrolled; neurosurgical intervention was performed in 34 patients (2.1%) and positive CT findings were demonstrated in 218 patients (13.8%); sensitivity and specificity for need for neurosurgical intervention were 100% (95% CI 90% to 100%) and 60% (95% CI 44% to 76%) for the CCHR and 82% (95% CI 69% to 95%) and 26% (95% CI 24% to 28%) for the NOC; negative predictive values for the above mentioned clinical decision rules were 100% and 99% and positive values were 5% and 2%, respectively, for the CCHR and NOC; Sensitivity and specificity for clinically significant head CT findings were 95% (95% CI 92% to 98%) and 65% (95% CI 62% to 68%) for the CCHR and 86% (95% CI 81% to 91%) and 28% (95% CI 26% to 30%) for the NOC	~30% did not receive CT head and proportion followed up not described; thus, major limitation from Design 1 to Design 3
Probst et al[54] (2020)	III for Q1	Prospective cohort study; multi-center	Adult patients with blunt head trauma who underwent neuroimaging in the ED Primary outcome was significant intracranial injury; secondary outcome neurosurgical intervention	N=9,070 15% (N=1,323) were anticoagulated Relative risk of significant intracranial injury was 1.3 (95% CI 0.9 to 1.9) for patients using aspirin alone, 0.8 (95% CI 0.2 to 2.3) for those using clopidogrel alone, and 1.9 (95% CI 1.3 to 2.8) for those using warfarin alone	Planned secondary analysis; concern for work-up bias as CT ordered by physicians but not stipulated by protocol; potential for selection/spectrum bias

Evidentiary Table (continued). 1388

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Easter et al[57] (2013)	III for Q1	Prospective cohort study at 1 urban academic ED	Consecutive adult patients (18 y or older) with intoxication and minor head injury All participants received head computed tomography Primary outcome was clinically important intracranial injury; secondary outcome neurosurgical intervention	N=283 Clinically important injuries were identified in 8% (N=23) with 0.4% (N=1) requiring neurosurgical intervention NEXUS criteria and the Canadian CT Head Rule had sensitivities of 83% and 70%, respectively	Limited sample size and indirectly applicable to question population; although described as consecutive, potential selection/work-up bias
Nishijima et al[70] (2012)	II for Q2	Multicenter prospective observational study	≥18 y patients with blunt head trauma on warfarin or clopidogrel regardless of LOC; looked for delayed ICH at 14-day follow-up; in 930 patients with initial normal head CT, delayed ICH occurred 4 of 687 (0.6%, 95% CI 0.2 to 1.5%) for warfarin, and 0 of 243 (0%, 95% CI 0 to 1.5%) for clopidogrel; of the 4, 2 died, none had neurosurgical intervention	83% of eligible patients were enrolled; 43 of 1,064 patients were on aspirin; 1 patient who died in clopidogrel group lost to follow up	Only delayed hemorrhage was in warfarin patients; although a few patients had delayed hemorrhage, and 2 of 930 died, none received neurosurgical intervention
Menditto et al[71] (2012)	III for Q2	Prospective case series at trauma center	>14 y with minor head injury with initial negative CT head, repeat before CT at 24 h	5 of 87 (6%) patients had positive second CT, 1 had craniotomy	No blinded outcome assessment or adjudication of outcomes; small sample; single institution; ~10% refused second CT head

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Cipriano et al[72] (2018)	III for Q2	Single center prospective observational study	Patients with mTBI age >18 y on oral anticoagulants	3 of 178 (1.7%) showed delayed ICH, 1 died (0.6%), no interventions	Small sample; small lost to follow-up; not generalizable
Kaen et al[73] (2010)	III for Q2	Prospective at single center	Mild head injury patients on anticoagulation with initial CT negative	2 of 137 (1.4%) patients showed hemorrhagic changes but did not need surgery or treatment	Small sample; unclear selection; single institution
Subbian et al[79] (2016)	III for Q3	prospective observational study of mTBI patients presenting to an urban ED	A chief complaint of head injury within the preceding 24 h were screened for inclusion from March 2013 to April 2014; the enrollment criteria were as follows: 1) age of 18 y or greater, 2) ability and willingness to provide written informed consent, 3) blunt head trauma and clinical diagnosis of isolated mTBI by the treating physician, and 4) blood alcohol level of <100 mg/dL; eligible mTIB patients were enrolled and their neuromotor function was assessed in the ED using a battery of 5 tests that cover a range of proprioceptive, visuomotor, visuospatial, and executive function performance metrics; at 3 wks postinjury, participants were contacted via telephone to complete the Rivermead Post-Concussion Symptoms Questionnaire to assess the presence of significant PCS	A total of 66 mTBI patients were enrolled in the study with 42 of them completing both the ED assessment and the follow-up; 40 patients were included in the analyses; the area under the receiver operating characteristic curve (AUC) for the entire test battery was 0.72 (95% CI 0.54 to 0.90); the AUC for tests that primarily measure visuomotor and proprioceptive performance were 0.80 (95% CI 0.65 to 0.95) and 0.71 (95% CI 0.53 to 0.89), respectively	Good methodology, but very small single-center study

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Sheedy et al[81] (2009)	III for Q3	Prospective case series from single hospital in Australia	Brief measures of neuropsychological functioning, acute pain, and postural stability were collected in the ED; telephone follow-up at 3 mos using the Rivermead Post-Concussion Symptoms Questionnaire was undertaken	Neuropsychological deficits, acute pain, and postural instability in the ED were significantly associated with postconcussive symptoms at 3-mo follow-up; a regression formula using 3 easily obtainable measures obtained during acute stage of injury—immediate and delayed memory for 5 words and a visual analog scale score of acute headache—provided 80% sensitivity and 76% specificity for the prediction of clinically significant symptoms at 3 mos postinjury	Small single center study, mainly a convenience sample
Booker et al[82] (2019)	III for Q3	Observational cohort study of larger database	SHEFfield Brain Injury after Trauma (SHEFBIT) cohort with mTBI in the ED were analyzed as part of the study; persistent PCS and long-term disability were measured using the Rivermead Post-Concussion Questionnaire and the Rivermead Post-Injury Follow-up Questionnaire	647 patients were recruited with a follow-up rate of 89%; Non-attenders were older (P <0.001), a greater proportion were retired (P <0.001) and had a greater burden of comorbidity (P=0.009); multivariate analysis identified that female gender, previous psychiatric history, GCS <15, aetiology of assault and alcohol intoxication, were associated with worse recovery	Data dredged study derived from larger database and different primary study

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Kraus et al[83] (2009)	III for Q3	Prospective cohort 5 hospitals in Southern California	Two cohorts, one with mTBI (N=689 at initial assessment) and another with non–head injuries (N=1,318); Rivermead Post-Concussion Symptoms Questionnaire and Pittsburgh Sleep Quality Index at 3 mos postinjury	Post-concussion symptom rates and summary Rivermead Post-Concussion Symptoms Questionnaire scores were significantly higher for persons with mTBI than for the comparison cohort; women reported significantly more symptoms than men; complaints about sleep quality overall (and also sleep latency and daytime dysfunction subcomponents) were significantly more frequent among those with mTBI	Primarily descriptive
Ponsford et al[84] (2019)	III for Q3	NET trial (29) examined the effectiveness of an implementation intervention to increase uptake of 3 recommendations for management of mTBI patients in EDs: (*i*) prospective assessment of posttraumatic amnesia using a validated tool; (*ii*) use of guideline-developed criteria to determine use and timing of CT imaging; and (*iii*) provision of written patient information upon discharge from the ED; This is a "brief overview" of the NET-plus component; 31 Australian EDs	343 individuals with mTBI completed the Rivermead Post-Concussion Symptom Questionnaire, Hospital Anxiety Depression Scale–Anxiety Scale, and Quality of Life–Short Form an average 7 mos post-injury	18.7% of participants reported 3 or more postconcussional symptoms, most commonly fatigue (17.2%) and forgetfulness (14.6%); clinically significant anxiety was reported by 12.8%, and was significantly associated with symptom rreporting, as were mental and physical quality of life scores; significant predictors of postconcussional symptoms at follow-up were pre-injury psychological issues, experiencing LOC, and having no recall of receiving information about brain injury in the emergency department	Incomplete methodology, analysis of subcomponent of larger trial

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Ponsford et al[85] (2012)	III for Q3	Secondary analysis of an ongoing prospective study examining use of a revised version of the Westmead posttramuatic amnesia Scale as a screening tool in patients with mTBI	123 patients with mTBI and 100 trauma patient controls recruited and assessed in the emergency department and followed up 1 wk and 3 mos postinjury; Outcome was measured in terms of reported post-concussional symptoms; measures included the ImPACT Post-Concussional Symptom Scale and cognitive concussion battery, including Attention, Verbal and Visual memory, Processing Speed and Reaction Time modules, pre- and postinjury SF-36 and MINI Psychiatric status ratings, Visual Analogue Scale Pain Inventory, Hospital Anxiety and Depression Scale, PTSD Checklist–Specific, and Revised Social Readjustment Scale	mTBI predicted post-concussional symptoms 1 wk postinjury, along with being female and premorbid psychiatric history, with elevated HADS anxiety a concurrent indicator; however, at 3 mos, preinjury physical or psychiatric problems but not mTBI most strongly predicted continuing symptoms, with concurrent indicators including HADS anxiety, PTSD symptoms, other life stressors and pain; HADS anxiety and age predicted 3-mo PCS in the mTBI group, whereas PTSD symptoms and other life stressors were most significant for the controls; cognitive measures were not predictive of PCS at 1 wk or 3 mos	Inadequate methodology, secondary analysis of larger study, no generalizability, data dredged

Evidentiary Table (continued).

Study & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Scheenen et al[86] (2017)	III for Q3	Sub-study of a larger prospective cohort study from three level 1 trauma centers in the Netherlands	Study aimed to compare patient characteristics and their associations with persistent post-concussive syndrome; endpoints were collected at 2 wks following injury and included standardized instruments	N=820; gender, psychiatric history, and psychological illness, including depression and anxiety, as well as post-traumatic stress were associated with post-concussive syndrome	Sub-study, but prospective; 2 wk follow-up may be limited
Su et al[87] (2014)	III for Q3	Prospective cohort study from 4 institutions in China	mTBI patients; plasma high-sensitivity C-reactive protein levels measured at baseline, 1-, 2-, and 3-mos follow-up; endpoints included persistent post-concussive syndrome, psychological problems (depression and anxiety), physiological problems), and cognitive impairment as measured by standardized instruments	N=213; multiple regression demonstrated significant associations between C-reactive protein and post-concussive syndrome, psychological problems, and cognitive impairment	Small sample; <10% lost to follow-up
Lange et al[88] (2015)	III for Q3	Prospective cohort study performed at Level 1 Trauma Center in Canada	Goal of this study was to estimate relationships between white matter changes, as measured by diffusion tensor imagining and post-concussive syndrome	N=108; 72 with mTBI and 36 trauma controls; no significant differences in diffusion tensor imaging measures and outcomes	Small sample but with comparative, control, group; diagnostic modality likely not available in ED setting

CCHR, Canadian Head CT Rule; *CI*, confidence interval; *CT*, computed tomography; *ED*, emergency department; *GCS*, Glasgow Coma Scale; *HADS*, Hospital Anxiety and Depression Scale; *ICH*, intracranial hemorrhage; *LOC*, loss of consciousness; *mo*, month; *mTBI*, mild traumatic brain injury; *NOC*, New Orleans Criteria; *PCS*, post-concussive syndrome; *PTSD*, posttraumatic stress disorder; *wk*, week; *y*, year.