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REVIEW ARTICLE

Systematic Review of the Clinical Course, Natural History, and Prognosis for Pediatric Mild Traumatic Brain Injury: Results of the International Collaboration on Mild Traumatic Brain Injury Prognosis

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Abstract

Objective: To synthesize the best available evidence on prognosis after pediatric mild traumatic brain injury (MTBI).

Data Sources: We searched MEDLINE, Embase, PsycINFO, CINAHL, and SPORTDiscus (2001−2012), as well as reference lists of eligible articles, and relevant systematic reviews and meta-analyses.

Study Selection: Controlled trials and cohort and case-control studies were selected according to predefined criteria. Studies had to have a minimum of 30 MTBI pediatric cases. After 77,914 records were screened for the entire review, 299 studies were eligible and assessed for scientific rigor.

Data Extraction: Eligible studies were critically appraised using the Scottish Intercollegiate Guidelines Network (SIGN) criteria. Two reviewers independently reviewed each study and extracted data from accepted articles into evidence tables.

Data Synthesis: Evidence from 25 accepted articles was synthesized qualitatively according to SIGN criteria, and prognostic information was prioritized according to design as exploratory or confirmatory. Most studies show that postconcussion symptoms and cognitive deficits resolve over time. Limited evidence suggests that postconcussion symptoms may persist in those with lower cognitive ability and intracranial pathology

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on neuroimaging. Preliminary evidence suggests that the risk of epilepsy is increased for up to 10 years after MTBI; however, there is insufficient high-quality evidence at this time to support this link.

Conclusions: Common post-MTBI symptoms and deficits in children are not specific to MTBI and appear to resolve with time; however, limited evidence suggests that children with intracranial pathology on imaging may experience persisting symptoms or deficits. Well-designed, long-term studies are needed to confirm these findings.

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Mild traumatic brain injuries (MTBIs) are common in children and adolescents. It is estimated that as many as 500,000 children younger than 15 years sustain TBIs that require hospital-based care in the United States, and most of these injuries are mild in severity.[1] A national cross-sectional study in the United States estimated that 1 of every 220 pediatric patients seen in emergency departments receive a diagnosis of MTBI.[2] Physical, emotional, behavioral, and cognitive symptoms such as headache, sleep disturbance, disorders of balance, fatigue, irritability, and memory and concentration problems commonly occur after MTBI. Knowledge about the course of recovery is important because it allows clinicians to provide appropriate advice to patients and families, and to identify patients at risk for poor recovery. Persistent symptoms or deficits after MTBI may lead to substantial functional disability interfering with children's academic performance or quality of life.

In a large systematic review[3] of MTBI prognosis published in 2004, the World Health Organization (WHO) Collaborating Centre for Neurotrauma, Prevention, Management and Rehabilitation Task Force found consistent evidence that children's prognosis after MTBI is good, with quick resolution of symptoms and cognitive deficits (within 3mo), and little evidence of MTBI-specific residual cognitive, behavioral, or academic deficits. The Task Force also found similarities between children sustaining an MTBI and those sustaining other kinds of injuries (eg, orthopedic), suggesting that where deficits are observed, they were likely due to premorbid characteristics or the experience of sustaining an injury in general, or both.

Understanding the course of recovery and identifying potential prognostic factors affecting recovery after MTBI in children are important for effective management and rehabilitation. The objective of this review is to update the WHO Collaborating Centre Task Force findings by synthesizing the best available evidence on the clinical course, natural history, and prognosis after MTBI in children. This review does not include psychosocial outcomes such as behavioral, emotional, psychological, or psychiatric outcomes, or family functioning. These outcomes are reported in another article in this supplement.[4]

Methods

Protocol registration

Our review was conducted and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[5] In accordance with the statement, our systematic review protocol was registered in the International Prospective Register of Systematic Reviews[6] on July 11, 2011, and was last updated on November 2, 2012 (registration no. CRD42011001410). We also published the protocol for our review.[7]

Search strategy

The literature search and critical review strategy are outlined in detail elsewhere[7] and in this special issue.[8] Briefly, the electronic databases MEDLINE, PsycINFO, Embase, CINAHL, and SPORTDiscus were systematically searched from January 1, 2001, to February 10, 2012. The search terms included *craniocerebral trauma*, *prognosis*, and *children* among others. The full search strategy can be found in the published protocol by Cancelliere et al.[7] The reference lists of all reviews and meta-analyses relating to MTBI, and articles meeting the eligibility criteria were screened for additional potentially relevant articles that may have been missed by our electronic searches. Additionally, members of the International Collaboration on MTBI Prognosis provided information about studies that they had knowledge of but were not found in the databases or reference lists.

Selection of articles

Articles were screened for eligibility according to predefined criteria. Inclusion criteria included original, published peer-reviewed research reports in English, French, Swedish, Norwegian, Danish, and Spanish. Studies had to have a minimum of 30 pediatric MTBI cases and had to assess outcomes such as post-concussion symptoms and cognitive deficits. Psychosocial outcomes such as behavioral, emotional, psychological, or psychiatric outcomes, or family functioning are discussed in another article in this supplement.[4]

Eligible study designs were controlled trials, cohort studies, and case-control studies. Exclusion criteria included study designs such as cross-sectional studies, and case reports and series, as well as cadaveric, biomechanical, and laboratory studies.

Case definition

Studies had to state a clear definition for MTBI, consistent with the definitions provided by the WHO Collaborating Centre Task Force and the Centers for Disease Control and Prevention (CDC). The WHO Task Force defines MTBI as "an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include (1) one or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; and (2) Glasgow Coma Scale score of 13−15 after 30 minutes postinjury or later upon presentation for healthcare. These manifestations of MTBI must not be due to drugs, alcohol, medications, caused by other injuries or treatment for other injuries, (eg, systemic injuries, facial injuries, or intubation), caused by other problems (eg,

psychological trauma, language barrier, or coexisting medical conditions) or caused by penetrating craniocerebral injury."[9] Persons with fractured skulls were included if they fit this case definition. The CDC provides an additional definition that can be derived from clinical records. According to the CDC, MTBI is present if an Abbreviated Injury Severity Scale score of 2 for the head region is documented.[10] An administrative data definition for surveillance or research is also provided.[10] Specifically, cases of MTBI are recognized among persons who are assigned certain *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnostic codes.[7]

Assessment of methodological quality

All eligible articles were critically appraised using a modification of the Scottish Intercollegiate Guidelines Network (SIGN) criteria.[11] A full description of the modifications to the SIGN criteria is found in our published protocol.[7] For example, we added a section to describe the main strengths and weaknesses of the study. Two reviewers performed independent, in-depth reviews of each eligible study to assess the impact of any biases on the results. A third reviewer was consulted for disagreements. Similarly, 2 reviewers independently extracted data from accepted articles into evidence tables, and the evidence was synthesized according to the modified SIGN criteria.

Synthesis of evidence

We performed a best-evidence synthesis. We also categorized the evidence on relevant prognostic factors as preliminary or confirmatory, using the phases of study framework described by Côté et al.[12] Phase I studies are hypothesis-generating investigations that explore the associations between potential prognostic factors and disease outcomes in a descriptive or univariate way. Phase II studies are extensive exploratory analyses that focus on particular sets of prognostic factors, or attempt to discover which factors have the highest prognostic value. Both phase I and phase II studies provide preliminary evidence. Lastly, phase III studies are large confirmatory studies of explicit prestated hypotheses that allow for a focused examination of the strength, direction, and independence of the proposed relationship between a prognostic factor and the outcome of interest. Information from accepted phase III studies is considered the strongest evidence, followed by evidence from accepted phase II studies. Phase I studies do not consider confounding factors and are considered more limited evidence.

List of abbreviations:

CDC	**Centers for Disease Control and Prevention**
CI	**confidence interval**
CT	**computed tomography**
GCS	**Glasgow Coma Scale**
GOS	**Glasgow Outcome Scale**
MTBI	**mild traumatic brain injury**
OI	**orthopedic injury**
OR	**odds ratio**
RR	**relative risk**
SIGN	**Scottish Intercollegiate Guidelines Network**
TBI	**traumatic brain injury**
WHO	**World Health Organization**

Results

Of 77,914 records screened for our entire review, 2170 full-text articles were assessed for eligibility.[8] Twenty-five publications addressing the clinical course, natural history, and prognostic factors in children were accepted as scientifically admissible (table 1). These studies form the basis of our best-evidence synthesis. We accepted 24 cohort studies from 19 unique samples, of which 3 were phase III studies, 6 were phase II studies, and 10 were phase I studies. One phase II case-control study was also accepted. Ten studies were conducted in the United States, 3 in Canada, 2 in Denmark, 2 in Australia, 1 in Germany, 1 in the United Kingdom, and 1 in Italy. Follow-up periods varied, with 13 studies following up patients for more than 3 months, 2 studies following up patients between 1 and 3 months, and 5 studies following up children for less than 1 month.

Clinical outcomes

Risk of epilepsy after MTBI in children

Using data from the Danish National Hospital Register, Christensen et al[13] (phase III) compared the relative risk of developing epilepsy between children with MTBI and those without head injury (see table 1). They found that the risk of epilepsy is increased after MTBI in children while controlling for age and sex. Children with MTBI are approximately twice as likely to develop epilepsy compared with children without MTBI (relative risk [RR]=2.22; 95% confidence interval [CI], 2.07−2.38). This risk is highest in the first year postinjury, but remains 50% higher in these children even 10 years post-MTBI (RR=1.51; 95% CI, 1.24−1.85). The number of new cases of epilepsy per 1000 person-years for children with MTBI aged 0 to 5 years, 5 to 10 years, and 10 to 15 years was 1.64, 1.56, and 1.54, respectively, compared with .87 new cases for those patients without MTBI. The incidence of epilepsy is approximately 6-fold greater in those with both MTBI and a family history of epilepsy than in those with neither TBI nor a family history (RR=5.75; 95% CI, 4.56−7.27).

Sleep disturbances after MTBI in children

Tham et al[14] (phase III) examined the trajectory of sleep disturbances measured by parental report over a 24-month period in a cohort of children with TBI compared with control subjects with orthopedic injuries (OIs) (see table 1). Children with MTBI and no abnormalities on computed tomography (CT) scan or no CT performed were classified as MTBI I. Those children with MTBI and skull fracture were classified as MTBI II. Baseline (preinjury) sleep disturbances were reported to be higher in the MTBI I and II groups compared with the OI group. These sleep disturbances persisted to 24 months postinjury for children with OI and MTBI I and II. However, by 3 months postinjury, adjusted analyses showed that the change in sleep disturbance in children with MTBI was not statistically different than the change in sleep disturbance in children with OIs.

Postconcussion symptoms (somatic and cognitive) after MTBI

Several studies[15-22] assessed the course of postconcussion symptoms, with most of the studies being exploratory. In children with MTBI without intracranial abnormality on neuroimaging, symptoms appeared to resolve in most patients over time.[15-17] Anderson et al[15] (phase I) followed up a cohort of children with MTBI and

Table 1 Clinical outcomes in children after MTBI

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Cohort studies					
Phase III					
Christensen et al,[13] 2009; Denmark	Danish population born in Denmark between Jan 1, 1977, and Dec 31, 2002 Population-based cohort n=1,605,216	Danish children born in Denmark between Jan 1, 1977, and Dec 31, 2002	MTBI as diagnosed with ICD-8 850.99; ICD-10 S06.0. Diagnosis based on American Congress of Rehabilitation Medicine definition: direct head trauma that results in LOC, amnesia, confusion, disorientation, or focal temporary neurologic deficit. LOC no longer than 30min, GCS 14 or 15 after 30min, PTA ≤24h	Prognostic factor: TBI severity, age at injury, sex, length of hospital stay, family history of epilepsy Outcome: time to diagnosis of epilepsy (ICD-8 345 from 1977 to 1993 and ICD-10 G40, G41 from 1994 to 2002)	RR of epilepsy after MTBI (compared with no TBI) was 2.22 (95% CI, 2.07–2.38). The risk was highest during the 1st year after injury (for first 6mo: RR=5.46; 95% CI, 4.67–6.37) and decreased over time, but at 10y or more was still 1.51 (95% CI, 1.24–1.85). RR of epilepsy in patients with MTBI and family history of epilepsy was 5.75 (95% CI, 4.56–7.27), compared with no TBI and no family history of epilepsy.
Tham et al,[14] 2012; U.S.	ED patients or inpatients at participating hospitals (trauma and nontrauma) in Washington and Pennsylvania. Injury occurred between March 1, 2007, and Sep 30, 2008. n=729 with TBI (616 with MTBI; 510 with MTBI I, 106 with MTBI II) and n=197 with OI F/U: 3, 12, and 24mo	Children aged 2–17y admitted for TBI or OI. OI group selected through age and sex matching and involved isolated arm fractures.	MTBI: any period of transient confusion, disorientation, impaired consciousness, or amnesia <24h, or signs of other neurologic or neuropsychological dysfunction; lowest GCS score 13–15 at initial evaluation and GCS of 15 at discharge from ED or at 24h postinjury if hospitalized. MTBI classified into MTBI I: no CT abnormalities or in whom CTs were not performed; MTBI II: skull fracture without intracranial hemorrhage; and MTBI III: intracranial hemorrhage	Prognostic factors: MTBI I, II, or III; age, sex, race, insurance, household income Outcome: sleep disturbance as reported by parents on 1 item in the PedsQL	Baseline (preinjury) sleep disturbances by parent report were reported to be higher in the MTBI I and II groups compared with the OI group. These sleep disturbances persisted to 24mo postinjury for children with OI and MTBI I and II. However, by 3mo postinjury, adjusted analyses showed that the change in sleep disturbance in children with MTBI was not statistically different than the change in sleep disturbance in children with OI.
Fay et al,[18] 2010; U.S.	Children recruited from consecutive visits to the ED of 2 children's hospitals in Ohio MTBI=182 Control (OI)=99	Inclusion: aged 8–15y with MTBI (see definition) or OI (upper or lower extremity fractures with AIS ≤3 without MTBI). Included those with or without hospitalization,	Blunt head trauma resulting in LOC of ≤30min, or GCS 13–14, or ≥2 acute signs or symptoms of concussion as noted by medical personnel (transient neurologic deficits,	Prognostic factors: cognitive ability as assessed within 3wk postinjury by a single composite score composed of the following: WASI, WRAT-3, CVLT-C, VMI,	Hierarchical linear modeling indicated that ratings of PC symptoms were moderated jointly by cognitive ability and injury severity. Children of lower cognitive ability with a

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	Participation rates were 48% in MTBI group and 35% in OI group. F/U: 1, 3, and 12mo	intracranial lesions, or skull fractures on CT. Exclusion: for MTBI group, excluded if delayed neurologic deterioration. For both groups, excluded if neurosurgical or surgical intervention; any injury interfering with neuropsychological testing; hypoxia, hypotension, or shock associated with the injury; ethanol or drug ingestion; prior head trauma requiring medical treatment; premorbid neurologic disorder or mental retardation; injury resulting from abuse or assault; severe psychiatric disorder; contraindication for MRI	persistent PTA, vomiting, nausea, headache, diplopia, dizziness, disorientation, or other mental status changes) "Complicated" MTBI: defined as trauma-related intracranial abnormalities on MRI	and 3 subtests from the CANTAB Type of injury, complicated vs uncomplicated MTBI, race, SES, age at injury, parent rating of premorbid symptoms using the PCS-I symptoms, premorbid HBI cognitive symptoms and somatic symptoms Outcomes: PC symptoms using PCS-I and HBI (both parent and child rated)	"complicated" MTBI had greater PC symptoms than OI controls at 3mo according to parents' ratings. Cognitive ability moderated PC symptoms in the complicated MTBI group on both the child PCS-I total score and parent-rated HBI cognitive symptom score. No significant interactions were found for the HBI somatic symptom rating (parent or child).
Phase II studies					
Woodrome et al,[21] 2011; U.S.	Same cohort as Fay et al[18]—see above	Same cohort as Fay et al[18]—see above	Same cohort as Fay et al[18]—see above	Prognostic factors: type of injury, preexisting PC symptoms (parent report), imaging (for MTBI group), acute clinical status, coping (Coping Strategies Inventory) Outcome: PC symptoms as measured by PCS-I and HBI	Children's use of coping strategies was associated with PC symptoms. Emotion-focused strategies were associated with more symptoms, and problem-focused strategies were associated with fewer symptoms.
Taylor et al,[19] 2010; U.S.	Same cohort as Fay et al[18]—see above	Same cohort as Fay et al[18]—see above	Same cohort as Fay et al[18]—see above	Risk factors: MTBI or OI, MRI brain findings Outcomes: PC symptoms measured by HBI and PCS-I	Parent report measures: Initial group differences in somatic PC symptoms and counts of PC symptoms resolved by 12mo postinjury. Cognitive PC symptoms: Symptoms remained higher in MTBI than OI children 12mo after injury.

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
					Child report measures: Higher total counts of PC symptoms at 12mo in MTBI children than OI children. No group differences in measures of somatic or cognitive PC symptoms at 12mo Higher levels of PC symptoms in the MTBI group were associated with motor vehicle trauma, LOC, neuroimaging abnormalities, and hospitalization.
Yeates et al,[20] 2009; U.S.	Same cohort as Fay et al[18]—see above	Same cohort as Fay et al[18]—see above	Same cohort as Fay et al[18]—see above	Prognostic factors: LOC, GCS <15, other injuries, MTBI or OI, intracranial abnormalities on MRI brain, preinjury symptoms Outcomes: PC symptoms were assessed by using the PCS-I.	Finite mixture modeling identified 4 longitudinal trajectories of PC symptoms: (1) none (64% of MTBI, 79% of OI); (2) moderate persistent (12% MTBI, 15% OI); (3) high acute/resolved (15% MTBI, 5% OI); (4) high acute/persistent (9% MTBI, 1% OI) MTBI children were more likely than OI children to have patterns of high acute and persistent symptoms (OR=13.68; 95% CI, 1.75–106.74), with large acute increases in PC symptoms 2wk after injury that persisted for at least 1y. Presence of LOC, injuries to other body regions, nausea, dizziness, disorientation, and other mental status changes each gave higher overall odds of belonging to the high acute/persistent PC symptom group.
Rockhill et al,[23] 2010; U.S.	Records of children enrolled in the Group Health Cooperative of Puget Sound in Washington	Inclusion: children aged <15y, registered in the GHC for at least 1y before reference date, and no TBI in the year before	MTBI defined using CDC criteria: ICD-9-CM codes with <1h or no LOC and no traumatic intracranial lesions	Prognostic factors: MTBI. Models adjusted for the following covariates: sex, age, presence of physical injury requiring	MTBI group more likely to have physical injury during 6mo before or after the MTBI (OR=3.04), more likely to

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	State MTBI = 489 Controls = 1470 F/U: 3y	the reference date. MTBI group: diagnosed with MTBI during visits to ED, hospital, or outpatient clinic. Controls: randomly selected, matched to MTBI subjects by age, sex, and enrollment at time of reference date		medical attention within 6mo of MTBI reference data, chronic medical illness, total health care costs in the year before the TBI reference date, presence of psychological distress in the year before the TBI reference date, number of 6-month intervals for which subjects had data available in the study Outcome: psychological distress, as determined by psychiatric diagnosis, use of mental health services or psychiatric medication prescription. Costs reflected health care services provided for or paid for by GHC (direct costs only, no indirect costs)	have had psychological distress in the year before the MTBI (OR = 1.59), and more likely to have psychological distress in the 3y after MTBI (OR = 1.71). Children with MTBI have greater medical costs during the 3-y period after the injury than control subjects over the same period, after controlling for covariates and for psychological distress subsequent to the MTBI (OR = 1.46, 95% CI, 1.33—1.60). Psychological distress in the 3y after the reference date is also independently associated with increased costs after adjusting for covariates and for MTBI status (OR = 2.08; 95% CI, 1.88—2.30).
Gagnon et al,[22] 2005; Canada	Children admitted to Trauma Program of the Montreal Children's Hospital, McGill University Health Centre after an MTBI Controls (n = 34) were friends of children with MTBI. 34 MTBI patients enrolled. F/U: 1, 4, and 12wk postinjury	MTBI group: age 8—16y, consecutive admissions to hospital for MTBI over 12-mo period; normal neurologic examination at discharge. Control group: age, sex, and premorbid level of activity (using Activity Rating Scale) matched friends of the patients. Exclusions for both groups: prior TBI, documented medical diagnosis of learning or attention deficit disorder, regular use of Ritalin, attendance at a special school for learning or behavioral problems, preinjury or	American Congress of Rehabilitation Medicine definition of MTBI. At least 1 of the following: any LOC of 30min or less; any PTA <24h; GCS 13—15 within 30min of injury	Prognostic factor: presence of MTBI Outcome: children's level of self-efficacy (defined as an individual's belief and confidence in his/her ability to succeed in a satisfactory manner in physical activities), PAQ, Athletic Competence subscale of the Self-Perception Profile for children or adolescents, RPSQ	Although children with MTBI returned to their preinjury participation in physical activities and showed no decrease in athletic ability, they had less confidence in their physical abilities.

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
		postinjury comorbidities limiting the assessment of upper or lower extremity response time			
Phase I studies					
Anderson et al,[15] 2012; Australia	Consecutive admissions to the Mater Children's Hospital in Brisbane and the Royal Children's Hospitals in Brisbane and Melbourne n=205 MTBI=130 F/U: 6mo	Inclusion: (1) age 6–14y at time of injury; (2) admission to hospital for TBI; (3) documented period of altered consciousness Exclusion: previous documented neurologic, psychiatric, or developmental disorder; TBI as a result of suspected child abuse	MTBI: lowest GCS in 1st 24h between 13 and 15 and an absence of neurologic and radiologic abnormalities	Prognostic factors: age at injury, family and sociodemographic factors, preinjury function Outcomes: postinjury function at 6mo including adaptive functioning (VABS), executive function (BRIEF)	Children with MTBI did not show significant changes over 6mo in parent ratings of adaptive function, executive skills, and quality of life.
Blinman et al,[16] 2009; U.S.	Admissions to an urban children's hospital, over a 2-y period n=63 of 139 eligible for inclusion F/U: 2–3wk postinjury	Inclusion: GCS 14–15 on arrival at ED, ages 11–19y; with or without CT abnormalities Exclusion: penetrating injuries and those discharged home from the ED	MTBI: GCS 14–15 on arrival at ED	Prognostic factors: sex, reported LOC, prior concussion, or GCS 14 vs 15 Outcomes: symptom questionnaire of ImPACT test battery (22 symptoms on 7-point Likert scale)	At baseline (mean 2d after injury), 83.6% of children had abnormal symptom scores (>8 on the scale). Symptoms improved for most after 2–3wk F/U, but worsened for 7 of the 63. 49% showed abnormal symptom score (>8). Most common symptom at F/U was excess sleep. GCS did not predict symptoms.
Anderson et al,[24] 2005; Australia Anderson et al,[25] 2005; Australia	Pediatric admissions to neurosurgical ward at Royal Children's Hospital, Melbourne, Australia, because of TBI n=42 with MTBI F/U: 30mo	Inclusion: age of injury 3y to 12y 11mo; admission to hospital; documented evidence of TBI including period of altered consciousness; completion of acute, 12-mo, and 30-mo evaluations Exclusion: penetrating head injury, previous TBI; TBI as a result of abuse; preexisting physical, neurologic, psychiatric, or developmental	Admission GCS of 13–15, no CT/MRI abnormality, no neurologic deficits	Prognostic factors: preinjury child and family functioning Outcomes: GOS used to determine physical outcome. Adaptive functioning (VABS)	For physical function, 97.6% of MTBI patients had good recovery at 30mo. There were no significant differences over time in functional domains. Functional deficits: At the acute stage, 83.3% had no deficits, 14.3% had 1 deficit, and 2.4% had 2 deficits. At 30mo, 90.5% had no deficits, 9.5% had 1 deficit. Age at injury did not predict outcomes.

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Table 1 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
		disorder			
Hawley et al,[32] 2004; United Kingdom	Children in the catchment area of the North Staffordshire Hospital NHS Trust; identified on the Head Injury Registry, which is linked to the Trauma Centre. Nov 1991 to Dec 1998 n=526 with TBI (419 with MTBI) 45 controls without injury F/U: mean of 2.2y (range, 0–5y)	Children with head injury discharged from acute hospital care Controls were identified by families of injured children. The families were asked to give details of a child without history of TBI, and of the same age and sex as the injured child.	Head injury causing unconsciousness for <15min, GCS after initial resuscitation of 13–15	Prognostic factors: TBI vs control; social deprivation index; other injuries Outcome: KOSCHI scores, as completed by parents: death, vegetative, severe disability (more vs fewer deficits), moderate disability (more vs fewer deficits), and good recovery (more vs fewer deficits)	No MTBI patients had severe disability. 43.2% had moderate disability according to the KOSCHI (8.1% with more symptoms and 35.1% with fewer symptoms), and 56.8% had good recovery (35.6% with more symptoms and 21.2% with fewer symptoms)
Korinthenberg et al,[17] 2004; Germany	Admissions to Manheim Children's Hospital over an 8-mo period n=98 F/U: 4–6wk	Inclusion: children aged 3–13y with mild head injury with duration of LOC <10min or no LOC; able to answer questions at time of admission; no complications necessitating intensive care or giving rise to a diagnosis of contusion or intracranial hemorrhage; age at least 3y; child and parents able to speak German, at least 1 parent available for interview within 24h of admission to hospital, informed written consent	Head injury with LOC <10min or no LOC	Prognostic factors: neurologic exam findings according to the "Examination of the Child with Minor Neurologic Dysfunction" (scores 0–2); structured interview with parent about history, physical and psychological development and behavior of child; sum of scores reflecting severity of trauma, somatic symptoms; EEG findings Outcomes: somatic symptoms, EEG findings	In the first 24h, nearly all children reported acute symptoms of concussion (93% with headaches), 38% had moderately to distinctly abnormal neurologic findings (mainly fine motor coordination and sensorimotor function), 65% had EEG abnormalities. At 4–6wk, 23% still had symptoms (16% had headaches); 10% still showed slight or moderate EEG abnormalities. There was no association between the EEG or neurologic findings at baseline and the persistent somatic complaints at F/U.

Abbreviations: AIS, Abbreviated Injury Scale; BRIEF, Behavior Rating Inventory of Executive Function; CANTAB, Cambridge Neuropsychological Testing Automated Battery; CT, computed tomography; CVLT-C, California Verbal Learning Test–Children's Version; ED, emergency department; EEG, electroencephalogram; F/U, follow-up; GCS, Glasgow Coma Scale; GHC, Group Health Cooperative; GOS, Glasgow Outcome Scale; HBI, Health and Behavior Inventory; ICD, *International Classification of Diseases*; ICD-9-CM, *ICD, 9th Revision, Clinical Modification*; ImPACT, Immediate Postconcussion Assessment and Cognitive Testing; KOSCHI, King's Outcome Scale for Childhood Injuries; LOC, loss of consciousness; MRI, magnetic resonance imaging; OI, orthopedic injury; OR, odds ratio; PAQ, Physical Activity Questionnaire; PC, post-concussion; PCS-I, Postconcussive Symptom Interview; PedsQL, Pediatric Quality of Life Inventory; PTA, posttraumatic amnesia; RPSQ, Rivermead Postconcussion Symptoms Questionnaire; RR, relative risk; SES, socioeconomic status; VABS, Vineland Adaptive Behavior Scale; VMI, Developmental Test of Visual-Motor Integration; WASI, Weschler Abbreviated Scale of Intelligence; WRAT-3, Wide Range Achievement Test–3rd edition.

without neuroimaging abnormalities, and reported that this cohort did not show significant deficits at 6 months postinjury in parent ratings of adaptive function, executive skills, and quality of life, compared with parents' reports of preinjury status, measured shortly after the injury (see table 1).

A different pattern of recovery for children with MTBI and intracranial abnormalities on imaging is suggested by a series of 4 reports based on a single cohort. These studies[18-21] assessed postconcussion symptoms using a cohort of children 8 to 15 years of age recruited from 2 emergency departments in Ohio. This group of children was followed longitudinally up to 12 months after injury along with a control group of children with uncomplicated OIs. Fay et al[18] (phase III) found that ratings of postconcussion symptoms were moderated jointly by cognitive ability and injury severity (see table 1). Cognitive ability, assessed by a single composite score of various psychometric tests within 3 weeks of injury, was considered to be a proxy of cognitive reserve capacity. Children of lower cognitive ability who had trauma-related intracranial abnormalities on magnetic resonance imaging of the brain ("complicated MTBI") had more postconcussion symptoms at 3 months (as reported by both the children and their parents) than a comparison group of children with OIs. Taylor et al[19] (phase II) found that the same group of children with MTBI had more parent-reported cognitive symptoms at 1 year after injury than children with OIs, but there were no differences in parent-reported somatic symptoms or total number of symptoms (see table 1). When the children themselves were asked, they reported a higher total number of symptoms (cognitive, emotional, and somatic) 1 year after injury. Several injury characteristics that reflected a greater severity of MTBI were predictive of higher levels of postconcussion symptoms in children with MTBI; these included loss of consciousness and neuroimaging abnormalities. Yeates et al[20] (phase II) used developmental trajectory analysis to classify the above cohort of children in terms of their patterns of postconcussion symptoms over time and identified 4 longitudinal trajectories: no postconcussion symptoms, moderate and persistent symptoms, high acute/resolved symptoms, and high acute/persistent symptoms (see table 1). Most children with MTBI (64%) did not display significant increases in symptoms measured by parental report (compared with parents' report of preinjury status) within 3 weeks of the injury. Children with MTBI were more likely than OI controls to have patterns of high acute and persistent symptoms at follow-up of 1 year (9% of children with MTBI vs 1% of children with OIs).

Health care costs after MTBI

There is limited evidence from 1 cohort study[23] (phase II) that health care costs of children with MTBI are higher than those of noninjured controls for 3 years after the injury (adjusted odds ratio [OR] = 1.46) (see table 1). This study followed up children enrolled in a health maintenance organization, comparing those with diagnosed MTBI with a matched sample of children without TBI. Children with MTBI were also almost 3 times more likely to have had a physical injury in the 6 months before or after the MTBI reference date (OR = 3.04), which suggests that children who sustain an MTBI are more "accident prone." Children with MTBI were also found to have had more psychological distress in the year before the MTBI reference date (OR = 1.59), which may suggest that children with psychological distress are at greater risk of MTBI. Furthermore, children with MTBI were found to have psychological distress in the 3 years after the MTBI reference date (OR = 1.71), which suggests that the relationship is reciprocal; that is, MTBI increases the risk of psychological distress. These findings should be considered preliminary and subject to confirmation in other cohorts.

Objective testing after MTBI: cognitive and motor outcomes

Eight studies[24-31] assessed cognitive and motor functioning after MTBI in children using objective tests of these measures. In a phase II cohort study, Babikian et al[26] found no difference in neuropsychological test performance between children with MTBI and injured non-TBI controls at 12 months postinjury, using various neuropsychological tests after adjusting for preinjury factors (table 2). However, both injured groups performed more poorly than healthy controls. However, there were no CT imaging data available for this study, so the findings must be interpreted with caution because this study does not stratify by the injury severity of the patients with MTBI (ie, intracranial abnormalities). Two phase I studies, Anderson et al[24,25] (see table 1) and Roncadin et al[27] (see table 2), assessed children with MTBI and no intracranial abnormalities and found no differences on neuropsychological test performance 1 year or more after the injury. In a phase II study of children with MTBI with and without abnormal CT imaging (ie, intracranial pathology, or "complicated MTBI"), Levin et al[28] found that at 12 months postinjury, those with intracranial pathology on CT (complicated MTBI) performed more poorly on neuropsychological testing compared with patients with normal CTs ("uncomplicated MTBI") (see table 2).

In a large population-based phase I study using linked data from a national database of hospitalizations and the draft board registry in Denmark, Teasdale and Engberg[29] reported that male draftees who had experienced a single concussion or MTBI (as identified by discharge *International Classification of Diseases* codes) between the ages of 12 and 17 years had increased odds of cognitive dysfunction on an objective cognitive test compared with the general population of draftees (OR = 1.42; 95% CI, 1.13−1.80) (see table 2). Those sustaining a single concussion ≤11 years of age showed no increased cognitive dysfunction compared with the general population. Those who had experienced 2 concussions or MTBIs had increased odds of cognitive dysfunction (OR = 1.46−1.59 at different age groups), but there was no relationship between age at injuries and cognitive dysfunction. The findings should be interpreted with caution because MTBI was ascertained through hospital admission records, which might suggest a greater severity of MTBI, although all concussion-related admissions were (by inclusion criteria) no more than 1 day. This study was also limited by the lack of clinical data on both preinjury risk factors (eg, learning disabilities) and injury variables such as the severity of the MTBI and neuroimaging data.

Gagnon et al[31] (phase II) studied 38 children aged 7 to 16 years with MTBI and found that on a functional measure of static and dynamic balance, children with MTBI performed more poorly at 12 weeks postinjury compared with a control group without MTBI (see table 2). This limited evidence suggests that children with MTBI may have balance and postural stability deficits up to 12 weeks postinjury.

Disability after MTBI

Two phase I studies[24,25,32] assessed disability after MTBI in children. Anderson et al[24,25] (phase I) assessed disability using the

Glasgow Outcome Scale (GOS)[33] to determine physical outcome in patients at 30 months post-MTBI. For physical function, 97.5% of patients with MTBI had good recovery at 30 months. The GOS is commonly used as an outcome measure for disability after MTBI. It classifies patients into 5 categories: dead, vegetative, severely disabled, moderately disabled, and good recovery (may include mild residual effects). However, the GOS is limited in its ability to distinguish mild disability and complete recovery.[34] In addition, since the definitions of the outcome categories relate to such items as independence in day-to-day living and return to work, it is not readily applicable to children and is likely to underestimate morbidity in this group.[34] Hawley et al[32] assessed disability post-MTBI at a mean follow-up period of 2.2 years (range, 0−5y) with the King's Outcome Scale for Childhood Injury[35] scores. There are 5 categories: death, vegetative, severe disability, moderate disability, and good recovery. No children with MTBI had severe disability, but a relatively high proportion had moderate disability (43%), which includes patients with temper outbursts, mood swings, memory problems, and learning difficulties. However, the findings of this study must be interpreted with caution because there was wide variability in follow-up, and the children in the study had been hospitalized, which suggests that this was a select sample with more serious MTBI. Another form of selection bias may be present in that the response rate was only 55.6%, leaving open the possibility that parents were more likely to respond if they identified their children as having problems. Furthermore, the reliability and validity of the King's Outcome Scale for Childhood Injury are not known.

Acute evaluation and triage of pediatric patients with MTBI

Five studies (2 phase II, 3 phase I)[36-40] examined the acute evaluation and triage of pediatric patients with MTBI. An important clinical concern in these patients is the detection of an underlying intracranial injury by neuroimaging that may ultimately require neurosurgical intervention. Vomiting is a common presenting complaint after head trauma and can be the basis for obtaining a head CT scan to rule out intracranial abnormalities.[41] Da Dalt et al[36] (phase II) studied the factors associated with vomiting after MTBI to ascertain its value in management decisions (table 3). They found that the presence of vomiting is significantly related to a personal or familial predisposition to vomit, rather than to the presence of an intracranial lesion. Halley et al[37] (phase I) studied the diagnostic value of physical examination for positive CT findings in patients with MTBI (see table 3). This study found that a standardized physical examination including a Glasgow Coma Scale (GCS) score has poor specificity and sensitivity in predicting intracranial injury on CT scan. The study findings had limited generalizability because the patient population was derived from a tertiary care center. Hollingworth et al[38] (phase II) studied the use of repeated head CT in pediatric MTBI to predict new and worsening brain injury (see table 3). In patients with MTBI, 19% had normal findings on initial CT scans. On a second CT scan, 20% had worsening findings. Overall, 1% (3/257) of patients with MTBI needed neurosurgical intervention. These 3 patients all had worsening findings on a second CT scan and had a marked decline in their GCS score within 7 hours of emergency department arrival. However, these patients recovered full neurologic function after surgery. The authors concluded that routinely obtaining a second CT scan is not necessary if patients have close neurologic assessment. Patients with MTBI at high risk for new or worsening brain injury on a second CT scan and subsequent neurosurgical intervention were those with an intraparenchymal brain injury on their first CT scan. This study is limited by the lack of a standardized protocol for performing a second CT scan of the head. Spencer et al[39] (phase I) evaluated the need for hospital admission in 197 patients admitted with MTBI (GCS score, 15) and a negative CT scan (see table 3). They did not find any delayed complications, defined as focal neurologic deficits, intracranial bleeding, worsening mental status, or recurrent seizures, during their hospitalization (mean length of stay, 2.9d; range, 1−24d).

Discussion

There were only 3 acceptable phase III studies that investigated prognosis after pediatric MTBI. Of the 19 unique cohorts of children with MTBI, almost 50% were phase I studies with the remainder being phase II or III. There is a significant paucity of confirmatory studies on the prognosis of pediatric MTBI. As a result, the evidence is limited and needs to be confirmed by additional research.

This review expands on the findings of the last systematic review[3] conducted by the WHO Collaborating Centre Task Force on MTBI in 2004. This WHO Task Force review concluded that children's prognosis after MTBI is good, with quick resolution of symptoms, usually within 2 to 3 months, and there is little evidence of residual cognitive or academic deficits. In our updated review, most studies report that postconcussion symptoms resolve over time when children are followed up to 30 months postinjury. There is limited evidence from 1 cohort of injured children suggesting that postconcussion symptoms may persist, especially for those children with lower cognitive ability and intracranial pathology on neuroimaging. These findings should be confirmed in other samples. Although most studies in this review reported no long-term, MTBI-specific cognitive deficits in children (which is consistent with the findings of the WHO Collaborating Centre Task Force), there was also limited evidence (from 1 exploratory study) that children with intracranial pathology may experience cognitive deficits up to 1 year postinjury. Well-designed, long-term studies are needed to confirm these findings.

The WHO Collaborating Centre Task Force review reported that there was an increased risk of epilepsy primarily in the first 4 years post-MTBI. In our updated review, a large population-based registry study showed that MTBI is a significant risk factor for the development of epilepsy.[13] Children with MTBI were approximately twice as likely to develop epilepsy postinjury as children without MTBI, and this risk was still increased 10 years after the injury. However, the absolute risk is low, with the number of new cases per 1000 person-years ranging from 1.55 to 1.64 for patients with MTBI $\leq$15 years of age compared with .87 cases for those with no MTBI. This study was limited by the lack of clinical information regarding the type or severity of epilepsy and the injury characteristics typically associated with posttraumatic epilepsy such as intracranial hemorrhage. Nevertheless, this study provides important information regarding risk estimates for epilepsy post-MTBI, particularly in terms of counseling patients with MTBI.

The WHO Task Force review did not accept any studies specifically designed to assess sleep problems in MTBI. We found 1 methodologically acceptable study by Tham et al[14] that found that children with MTBI have greater baseline (preinjury) sleep

Table 2 Objective outcomes (neuropsychological and motor) in pediatric MTBI

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Cohort studies					
Phase II					
Babikian et al,[26] 2011; U.S.	Admissions to 14 participating EDs in California Data collection started in 1989; interviews completed 1997 124 children with MTBI, 115 with other injuries, and 145 noninjured children F/U: 1, 6, and 12mo	All subjects were aged 8—17y. MTBI with AIS score of 1 or 2, no injuries in other sites in which the AIS score was >2, treated at one of the participating EDs, injury was through unintentional external cause, no litigation involved, no serious injury or death of others in the index injury, age 8—17y at time of injury, no significant preexisting central nervous system damage or serious chronic disease, consent of parent/guardian and child residing with parent/guardian Injured control group with non-head injuries from same EDs, matched to MTBI group on sex, age, ethnicity, SES and AIS; same inclusion criteria as MTBI. Children with injuries that would interfere with testing were excluded. Noninjured control group recruited from schools similar in demographics to injured groups; matched to MTBI group on sex, age, ethnicity, and SES	Head injury with AIS score of 1 or 2: LOC <1h, no neurologic deficit, GCS score of 13—15; for those with GCS score of 13 or 14, level of consciousness and sensorium improving in ED; with or without skull fracture	Prognostic factors: age, parent education Outcomes: memory (Prospective Memory Test, Picture Memory Test, Word List Memory Test); motor and psychomotor (Symbol Digit Modalities, Color Trails—Part B Child Version, Pin Test); attention/concentration inhibition (Span of Apprehension Test, Stroop Test—Interference Condition, Degraded Stimulus Continuous Performance Test); language (PPVT)	Both MTBI and non-MTBI injured groups performed more poorly than noninjured controls on tests assessing memory, psychomotor processing speed, and language. After adjusting for preinjury factors, the MTBI group showed no greater long-term neurocognitive impairment than the non-MTBI injured group.
Levin et al,[28] 2008; United States, Canada	Multicenter study of trauma centers in United States and Canada, 1998—2002 n=80 (32 with MTBI complicated by neuropathology on CT, 48 with normal CT findings or linear skull fracture only). F/U: 3, 6, and 12mo	Children aged 5—15y with MTBI, CT within 24h after injury Exclusions: evidence or history of child abuse, preexisting neurologic disorder, autism or schizophrenia, arrival at ED >24h after injury, penetrating brain injury Complicated MTBI (CMTBI): MTBI with intracranial pathology on CT head	MTBI: closed head trauma, lowest GCS score 13—15 at ED, altered or LOC not exceeding 30min	Prognostic factors: complicated vs uncomplicated MTBI, injury severity (AIS, ISS), SES, structured psychiatric interview or developmental questionnaire Outcomes: neuropsychological tests at 12mo for working memory, episodic memory, response inhibition, processing speed (WISC III), visuomotor speed, letter-word identification (WJTA), calculation (WJTA)	At 12mo, children with CMTBI performed more poorly on tests of episodic memory, processing speed, response inhibition, calculation ability, and letter-word identification when compared with uncomplicated MTBI patients. Among patients without a preinjury history of ADHD, CMTBI patients performed more poorly on working memory compared with uncomplicated MTBI patients.

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Table 2 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Gagnon et al,[30] 2004; Canada	Same cohort as Gagnon et al,[22] 2005 (table 1) n=40 MTBI patients n=38 with F/U at 1, 4, and 12wk postinjury	Same cohort as Gagnon et al,[22] 2005 (table 1)	Same cohort as Gagnon et al,[22] 2005 (table 1)	Prognostic factor: presence of MTBI Outcomes: response times using (1) the response speed subtest of the BOTMP and (2) an apparatus developed to measure reaction time and movement time for simple choice and reversed choice paradigms for upper and lower extremities	Children with MTBI had worse raw response speed scores on the BOTMP at 1wk only, and worse age-equivalent response speed scores on the BOTMP at 1wk and at 12wk, but not at 4wk compared with controls. There was no difference between groups on reaction, initial movement, and change of direction times on the response time apparatus.
Gagnon et al,[31] 2004; Canada	Same cohort as Gagnon et al,[22] 2005 (table 1)	Same cohort as Gagnon et al,[22] 2005 (table 1)	Same cohort as Gagnon et al,[22] 2005 (table 1)	Prognostic factor: presence of MTBI Outcomes: (1) balance subtest of the BOTMP; (2) P-CTSIB; (3) PST	Children with MTBI showed balance and postural stability deficits at 12wk postinjury compared with a noninjured control group.
Phase I studies					
Roncadin et al,[27] 2004; Canada	Children involved in research studies and clinical sources at the Hospital for Sick Children in Toronto n=126 with head injury (40 with MTBI) F/U: mean time ± SD since injury, 3.66±1.70y	Inclusion: school-aged children, who had been hospitalized for closed head injury; single injury at least 1y before testing, Verbal Performance IQ score >70 Excluded those with preexisting neurologic disorders associated with cerebral dysfunction and/or cognitive deficit, or inflicted or gunshot injury	GCS score 13–15 (modified GCS used for those aged <2y), LOC or disruption of consciousness <15min, no neurosurgical intervention, no imaging abnormalities other than linear skull fracture	Prognostic factors: age at injury, time since injury. Outcomes: Recognition Memory Test (auditory-verbal working memory task)	The distribution of working memory scores in children with MTBI is normal. Age at injury and time since injury did not predict working memory score.
Teasdale and Engberg,[29] 2003; Denmark	Danish population: Data source was National Bureau of Health registry of all hospitalization discharges in Denmark since 1979 and draft board register (conscription for all Danish men at age 18y).	Inclusions: males, admitted to hospital between 1979 and 1993, age <18y, born after 1968 (would appear before the draft board between 1987 and 2001). ICD-8 850 (concussion, admission to hospital for not more than 1d), 800, 801, 803 (cranial fracture); 851–854 (cerebral lesion); tested at 18y of age. Double concussion is defined as admission to hospital for concussion on 2 separate occasions.	MTBI defined as ICD-8 850	Prognostic factors: group membership: single concussion, double concussion, cranial fractures, cerebral lesion Outcomes: cognitive dysfunction as measured by a cognitive test called Borge Prien Prove (test for	Compared with the general population of draftees, those with a single concussion between ages of 12 and 17y have increased odds of cognitive dysfunction (OR=1.42; 95% CI, 1.13–1.80).

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Table 2 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
	n = 970 with single concussion, 521 with double concussion, 961 with cranial fractures, and 639 with cerebral lesions Mean age ± SD at testing: 19±1.2y	Excluded: those exempted from the draft for documented illnesses or conditions, which would disqualify them from military service		cognitive ability: logical, verbal, numerical, and spatial reasoning)	Those with double concussions have increased odds of cognitive dysfunction (OR = 1.46 −1.59 for different age groups), but there was no relation with age at injuries.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AIS, Abbreviated Injury Scale; BOTMP, Bruininks-Oseretski Test of Motor Proficiency; CMTBI, complicated mild traumatic brain injury; ED, emergency department; F/U, follow-up; ICD, *International Classification of Diseases*; IQ, intelligence quotient; ISS, Injury Severity Scale; LOC, loss of consciousness; P-CTSIB, Pediatric Clinical Test of Sensory Interaction for Balance; PPVT, Peabody Picture Vocabulary Test; PST, Postural Stress Test; SES, socioeconomic status; WISC-III, Weschler Intelligence Scale for Children—3rd edition; WJTA, Woodcock-Johnson III Tests of Achievement.

disturbances than children with OIs, and these sleep disturbances can last up to 2 years postinjury. However, by 3 months, there are no differences in sleep disturbance between the children with MTBI and those with OIs. This study was limited by the use of a nonvalidated subjective measure of sleep disturbance rather than a validated sleep questionnaire or use of an objective measure like actigraphy. Therefore, based on 1 phase III study, preliminary evidence suggests that there is no difference in sleep disturbance by parental report in pediatric patients with MTBI up to 24 months compared with patients with OIs. Further high-quality studies are needed to confirm this finding.

In 1 population-based phase I study,[29] patients admitted with an MTBI who previously have had an MTBI were found to have increased cognitive dysfunction compared with the general population when tested at 19 years of age. This suggests that there may be a cumulative effect of recurrent MTBI on cognitive function over time; however, there is insufficient high-quality evidence at this time to confirm this link. Well-designed confirmatory studies are needed to address this important issue.

One phase II study[31] reported that children with MTBI may have balance and postural stability deficits up to 12 weeks postinjury. This finding is preliminary and needs to be confirmed with additional studies. It suggests that the assessment of children's balance after MTBI may be important to ensure a safe return to sports or other activities that require high-level balance skills.

The decision to order a head CT scan for children with MTBI is critically important because of increasing concern over minimizing radiation exposure in children. One phase II study[38] reported that in patients with MTBI who require 2 head CT scans, 1% required neurosurgical intervention. Patients were at higher risk of neurosurgical intervention if there was intraparenchymal brain injury on the first CT scan and if there was neurologic deterioration. This finding is preliminary and needs to be confirmed by additional research. The study was limited by the lack of a standardized protocol for performing a second CT scan of the head. Intracranial injuries on CT that do not require surgical intervention may still have neurologic sequelae such as cognitive difficulties[19,20] and have important implications regarding the education of parents and children to monitor for school difficulties, and decisions on return to play.

Study limitations

Our findings are limited because of the lack of high-quality studies available in the literature. We found only 3 acceptable phase III studies on prognosis after MTBI in children: 1 study relating to the risk of epilepsy after MTBI, 1 study relating to the risk of sleep disorders post-MTBI, and another relating to the moderation of postconcussion symptoms by cognitive ability and injury severity. The paucity of confirmatory studies prevents firm conclusions about the role of predictors of recovery after MTBI. This highlights the need for well-designed, long-term confirmatory studies that account for potential confounders to understand the prognosis after pediatric MTBI.

Another limitation is that many studies recruited from hospital emergency departments or from patients admitted to the hospital. This limits the generalizability of the findings because many children with MTBI are seen as outpatients. Many measures of postconcussion symptoms ask the patients or parents to identify symptoms that are either new or more intense since the injury, and thus are likely affected by recall bias or reporting bias.

Table 3 Acute triage of children with MTBI

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
Case-control studies					
Phase II					
Da Dalt et al,[36] 2007; Italy	Children recruited from pediatric ED in a metropolitan area in Italy (Padova), of whom 45,000 are younger than 15y. 1248 admitted to hospital during a 1-y period, 1097 of whom were discharged home after MTBI. n=148 cases with vomiting; n=296 controls without vomiting. Time between exposure and outcome was 6mo.	Children aged <15y, admitted to pediatric ward after a blunt head trauma, previously healthy, normal results on initial and subsequent examinations, no subsequent complications. Cases were those who had vomiting before arrival or during the ED examination. Controls were those with minor head injury but without vomiting, matched by age group and discharged immediately before or after each case.	Temporary LOC (<1min) or immediate PTA, no basilar, depressed, or open fracture. Those with immediate posttraumatic seizure not excluded	Prognostic factors: personal and family history of recurrent vomiting, motion sickness, recurrent headache; personal history of recurrent abdominal or limb pain Outcome: case status (vomiting, no vomiting after MTBI)	Predictors of vomiting were (in multivariable analysis) personal history of recurrent vomiting (OR=5.90; 95% CI, 1.18–29.47), headache at time of injury (OR=4.37; 95% CI, 2.23–8.57), personal history of motion sickness (OR=2.34; 95% CI, 1.32–4.10), and number of recurrent problems in the family (OR=1.66, 95% CI, 1.29–2.13).
Cohort studies					
Phase II					
Hollingworth et al,[38] 2007; U.S.	Pediatric patients admitted to a level 1 trauma center in the United States for TBI between 1994 and 2003 and having more than 1 CT scan. Of 8505 pediatric patients with blunt trauma, 1203 had ≥2 CT scans. 521 met the other inclusion criteria; and 257 were MTBI. F/U: through surgery or discharge	Age <15y; acute blunt head trauma leading to hospital admission; 2 or more CT scans performed Exclusion criteria: penetrating head injury; no CT within 6h of ED arrival; ≤1 noncontrast head CT scan; craniotomy or ventriculostomy before the second head CT; transferred from another hospital; died in ED	GCS score 13–15 in the ED	Prognostic factors: laboratory studies, systolic blood pressure, GCS score, temperature, ICP (initial and worst values before second CT for each). For surgical patients, last GCS score and ICP before second CT, timing of surgery. Outcomes: (1) CT change defined as "worsening" (ie, new or worsening lesion) or "stable"; (2) need for neurosurgical intervention	In the MTBI group, 19% had normal findings on initial CT scan. On second CT, 20% had worsening findings. Overall, 1% (3/257) of MTBI patients needed neurosurgical intervention. These 3 patients all had worsening second CTs and had a marked decline in GCS score within 7h of ED arrival. Recursive partitioning analysis: the probability of new or worsening findings on second CT was 38% for those with any intraparenchymal finding on first CT; 11% with skull or facial fracture, EDH, SDH, SAH, or IVH; and 4% with normal findings on first CT. The probability of surgery

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Table 3 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
					after worsening second CT was 3% for those with any intraparenchymal finding and 0% for normal CT findings or other abnormalities on CT.
Cohort studies					
Phase I					
Halley et al,[37] 2004; U.S.	Catchment area of a large, tertiary pediatric trauma center in San Diego County, between Aug 24, 2001, and Sep 7, 2002 n=98 F/U: 4–6wk	Inclusion criteria: children aged 2–16y being evaluated at a pediatric trauma hospital for closed head injury with brief LOC or amnesia Excluded those aged <2y or >16y, did not have a witnessed LOC or amnesia, had a painfully distracting injury, were intoxicated, had history of prior neurologic abnormality, history suggestive of nonaccidental trauma, or were not to undergo head CT scan as part of their evaluation	Minor closed head trauma with GCS score on arrival at ED of 13–15; <5min LOC or amnesia	Prognostic factors: normal vs abnormal evaluation (normal evaluation: GCS score 15; no hematoma, step-off, or deformity on examination; hemotympanum not present; pupillary response brisk, reactive, and equal; awake, alert, and oriented, if applicable; motor strength strong and equal in all limbs; sensation present in all limbs) Outcome: intracranial/cranial injury on head CT, need for neurosurgical intervention, death	Standardized clinical exam does not adequately predict CT abnormalities in children with MTBI. Incidence of intracranial injury in entire group was 13.3% (95% CI, 7.9%–21.4%). 10.5% of those with normal findings on exam had positive CT; 15% of those with abnormal findings on exam had positive CT. Sensitivity, specificity, PPV, and NPV of clinical examination to detect CT abnormality were 69%, 40%, 15%, and 89%, respectively.
Spencer et al,[39] 2003; U.S.	Large urban level-1 trauma center with dedicated pediatric surgery services. Captured admissions for MTBI over 4y n=197 F/U: through discharge (mean length of stay, 2.9d; range, 1–24d)	Children aged ≤13y, admitted to the pediatric surgery service, MTBI	Blunt head trauma with GCS score 15, nonfocal findings on neurologic examination, negative head CT scan. (CT administered to those with LOC, amnesia, headache, seizure, nausea, vomiting, confusion, or sleepiness)	Prognostic factors: none Outcome: delayed complications (defined as focal neurologic deficits, intracranial bleeding, worsening mental status, recurrent seizures)	Pediatric patients with MHI and negative CT scans did not have delayed complications.
Grubenhoff et al,[40] 2011; U.S.	Children attending ED after concussion. n=348 (183 extremity injuries, 66 MTBI without AMS, and 99 MTBI with AMS, as defined in prognostic factors section) No follow-up past enrollment	Inclusion: age 6–18y with MTBI Excluded those who had received opioid pain medication before enrollment, had a history of intracranial surgery or neoplasm, developmental delay or	Blunt head trauma with GCS score 13–15, with or without abnormal CT findings	Prognostic factors: MTBI with AMS (AMS: GCS score 13 or 14 or any witnessed LOC or PTA); MTBI without AMS (GCS score 15, no LOC or PTA) Outcome: presence and severity of postconcussive	At enrollment in ED, those with AMS had more frequent and severe symptoms (median score, 10) than those with MTBI but no AMS (median score, 5) and those with extremity injuries (median

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Table 3 (*continued*)

Author, Year, Country	Source Population, Study Size, Participation, F/U	Inclusion/Exclusion Criteria	MTBI Case Definition	Prognostic Factors/Outcomes	Findings
		autism, structural brain abnormality, inborn error of metabolism, had evidence of an open skull fracture, or appeared to be intoxicated		symptoms, assessed using the Standardized Assessment of Concussion	score, 1). Headache, nausea, dizziness, blurred/double vision, and not feeling "sharp" were associated with MTBI with AMS.

Abbreviations: AMS, altered mental status; ED, emergency department; EDH, epidural hematoma; F/U, follow-up; ICP, intracranial pressure; IVH, intraventricular hemorrhage; LOC, loss of consciousness; MHI, mild head injury; NPV, negative predictive value; PPV, positive predictive value; PTA, posttraumatic amnesia; SAH, subarachnoid hemorrhage; SDH, subdural hematoma.

Conclusions

The best evidence on prognosis after MTBI in children suggests that postconcussion symptoms resolve over time in most children. There is limited evidence from 1 cohort suggesting that postconcussion symptoms may persist, especially for those children with lower cognitive ability and intracranial pathology on neuroimaging. These findings should be confirmed in other samples. Although most studies in this review reported no long-term, MTBI-specific cognitive deficits in children, there was also limited evidence from 1 exploratory study that children with intracranial pathology may experience cognitive deficits up to 1 year postinjury. Population-based data suggest that the risk of epilepsy is increased after MTBI in children even after 10 years postinjury. Preliminary evidence suggests that pediatric MTBI is not associated with significant changes in sleep disturbance over time compared with those with OIs. There is still a need for high-quality, phase III confirmatory studies on prognostic factors in children post-MTBI that will help inform evidence-based monitoring or rehabilitation of any persisting symptoms or deficits.

Keywords

Child; Craniocerebral trauma; Prognosis; Recovery of function; Rehabilitation

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