J Rehabil Med 2004; Suppl. 43: 84–105

Taylor & Francis
healthsciences

PROGNOSIS FOR MILD TRAUMATIC BRAIN INJURY: RESULTS OF THE WHO COLLABORATING CENTRE TASK FORCE ON MILD TRAUMATIC BRAIN INJURY

Linda J Carroll,[1] J. David Cassidy,[1,2,3] Paul M. Peloso,[4] Jörgen Borg,[5] Hans von Holst,[6] Lena Holm,[3] Chris Paniak[7] and Michel Pépin[8]

From the [1]Alberta Centre for Injury Control and Research, Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada, [2]Department of Medicine, University of Alberta, Edmonton, Alberta, Canada, [3]Section for Personal Injury Prevention, Department of Clinical Neurosciences, Karolinska Institutet, Stockholm, Sweden, [4]Department of Internal Medicine, University of Iowa, Iowa City, Iowa, USA, [5]Department of Rehabilitation Medicine, Uppsala University, Uppsala, Sweden, [6]Department of Neurosurgery, Karolinska Institutet, Division of Neuronic Engineering, Royal Institute of Technology, Stockholm, Sweden, [7]Glenrose Hospital and the Departments of Psychology and Educational Psychology, University of Alberta, Edmonton, Alberta, Canada, [8]Department of Psychology, Laval University, Quebec, Canada

We searched the literature on the epidemiology, diagnosis, prognosis, treatment and costs of mild traumatic brain injury. Of 428 studies related to prognosis after mild traumatic brain injury, 120 (28%) were accepted after critical review. These comprise our best-evidence synthesis on prognosis after mild traumatic brain injury. There was consistent and methodologically sound evidence that children's prognosis after mild traumatic brain injury is good, with quick resolution of symptoms and little evidence of residual cognitive, behavioural or academic deficits. For adults, cognitive deficits and symptoms are common in the acute stage, and the majority of studies report recovery for most within 3–12 months. Where symptoms persist, compensation/litigation is a factor, but there is little consistent evidence for other predictors. The literature on this area is of varying quality and causal inferences are often mistakenly drawn from cross-sectional studies.

Key words: mild traumatic brain injury, epidemiology, prognosis, recovery.

J Rehabil Med 2004; suppl. 43: 84–105

Correspondence address: Linda J Carroll, Department of Public Health Sciences, University of Alberta, 3080 RTF, 8308-114 St, Edmonton, AB, Canada, T6G 2E1.
E-mail: lcarroll@ualberta.ca

INTRODUCTION

The incidence of hospital-treated mild traumatic brain injury (MTBI) is high, at 100–300/100,000 population per year, making this a public health problem, disproportionately among teenagers and young adults (1). The outcome and course of recovery after MTBI is important to patients, healthcare professionals, researchers and policymakers, and impacts on decisions about compensation after an injury. Knowledge about the usual course of recovery after MTBI allows clinicians to provide appropriate advice to patients, and to recognize when recovery is not taking place as expected. Identification of premorbid and injury-related factors affecting recovery after MTBI may also help clinicians to screen individuals who are at greatest risk for sub-optimal outcome. However, there is great variability in opinions and research findings about prognosis after MTBI, as well as great variability in the quality of research.

The most informative studies of prognostic factors and outcome after MTBI employ a longitudinal design, and identify a comprehensive and representative cohort of subjects with MTBI as soon as possible after the injury. These individuals should then be followed over time to identify time to recovery, and prognostic factors affecting recovery or symptom persistence. Both cohort and case-control studies can be used to identify and test the strength of the association between potential prognostic factors and outcome.

Strength of the evidence within longitudinal studies also needs to be considered. One paradigm that has been used for ranking evidence of prognostic factors in breast cancer and whiplash classifies cohort studies into a 3-level hierarchy of knowledge (2, 3). Phase I studies explore associations between potential prognostic factors and disease outcomes in a descriptive way. For example, a cohort study exploring the crude relationship between age and recovery after MTBI is considered a phase I study. Phase II studies are more extensive exploratory studies using controls, stratified analyses and/or multivariable analyses to focus on sets of prognostic factors. For example, if a study of the association between age and recovery after MTBI is stratified by other factors thought to be important (such as positive or negative intracranial findings), it would be classified as a phase II study, since the association between age and recovery has considered the confounding of intracranial abnormalities. Phase III are confirmatory studies, where the goal is to confirm or refute the independence of the relationship between a particular prognostic variable and the outcome of interest. For example, a phase III study examining the strength and independence of the relationship between age (the exposure) and recovery after MTBI (the outcome of interest) would test that relationship while explicitly controlling for possible confounders of that relationship. A confounder is defined as a third factor that is associated with both the exposure and the outcome. It is not in the causal pathway between the exposure and the

DOI 10.1080/16501960410023859

outcome, but accounts for some or all of an observed relationship between that exposure and the outcome. In our example, this might involve examining the relationship between age and recovery from MTBI after explicitly controlling for such confounders as MTBI severity, pre-injury health, other injuries and others. Using this hierarchical framework, a phase I study might identify a potential prognostic factor for recovery from MTBI. A phase II study would explore that relationship further by also considering other possible prognostic factors. A phase III study would then confirm the strength and independence of that relationship, given a wide range of possible confounders. In the current paper, this hierarchy is employed to interpret the prognostic studies.

The main objective of the task force was to perform a systematic search of the literature on MTBI in order to produce a best-evidence synthesis on the epidemiology (incidence, risk and prevention), diagnosis, treatment and prognosis of MTBI. In this paper, we report the best-evidence regarding prognosis MTBI, and we identify factors that determine variations in prognosis. Our purpose was to create a baseline of the best scientific evidence that can inform clinicians, researchers and policymakers about MTBI.

METHODS

The literature search and critical review strategy is outlined in detail elsewhere (4). Briefly, we performed a systematic search of the world literature on MTBI using the following electronic databases: Medline and PsycINFO (1980–2000), Cinahal (1982–2000) and Embase (1988–2000), and screened these abstracts for relevance to the task force mandate. Articles were considered relevant if they examined diagnosis, incidence, risk factors, prevention, prognosis, treatment and rehabilitation or economic costs of mild traumatic brain injury; if they contained data and findings specific to MTBI; or if they described a systematic review of the literature on MTBI. We also checked reference lists from relevant articles and solicited literature from experts in the field of MTBI, and we report 2 original research studies performed as part of the task force mandate (5, 6). Rotating pairs of Scientific Secretariat members (listed at the front of this supplement) independently reviewed each article relevant to MTBI, identifying strengths and weaknesses and extracting data for our evidence tables. The Scientific Secretariat as a whole then discussed each article, and made a consensus judgement about its scientific merit (4).

We classified the cohort studies identifying prognostic factors into phase I, II or III studies, depending whether the associations were described in a descriptive or univariate way (phase I); described in a more extensive exploratory manner using comparisons with controls groups or multivariable approaches (phase II); or described in a confirmatory manner, in which the strength, direction and independence of a particular hypothesized prognostic factor is examined in a focused manner (phase III) (2, 3). Accepted articles are summarized in evidence tables and included in the best-evidence synthesis (7, 8), which follows. The best-evidence synthesis links summary statements and conclusions to the evidence tables so that the strength of the evidence on which these statements are based is obvious. Strength of the evidence considers both the design of the study and methodological quality. Information from sound phase III studies is confirmatory, and considered the strongest evidence, followed by evidence from methodologically sound phase II studies. Phase I studies do not consider confounding and are considered more limited evidence, but still potentially more informative about prognosis than cross-sectional and case series designs. Evidence from case series and cross-sectional studies is included in these summary statements, but carries less weight than more robust designs and is considered suggestive.

RESULTS

We found 427 articles in our literature search pertaining to prognosis of MTBI. After critically reviewing these studies plus the original research study pertaining to prognosis (5), we considered 120 (28%) to be of sufficient scientific merit to be accepted for our best-evidence synthesis. These studies are the basis for our findings and consist of 67 cohort studies, 2 case-control studies, 17 cross-sectional studies, 1 controlled trial of intervention identifying prognostic factors, 7 studies of diagnostic procedures relating to prognosis, 1 systematic review and 25 case series or other variant study designs. Of the cohort studies, 25 were phase I, 40 were phase II and 2 were phase III prognostic cohorts. The heterogeneity of the study populations, study designs, prognostic factors, follow-up periods, outcomes and analyses does not support statistical pooling of results, and therefore our findings are presented for each study in our evidence tables and form the basis for our recommendations.

Prognosis of mild traumatic brain injury in children

Twenty-eight longitudinal (9–36), 1 cross-sectional study (37) and 1 case series (findings reported in 2 publications) (38, 39) examined outcome and prognostic factors of MTBI in children (Table I). These studies included a variety of control groups; such as children with other injuries (11–13, 30, 34), children hospitalized for other reasons (37), healthy school children (9, 10, 14, 15, 18–20, 29, 35, 36), or 2 or more control groups (24, 26).

Post-concussion symptoms, cognitive and behavioural sequelae. Two phase II cohort studies indicate that post-concussion symptoms in children appear to be largely resolved within 2–3 months of the injury (13, 30) and the majority of studies report no short- or long-term cognitive problems, or post-injury behavioural deficits attributable to MTBI (9, 10, 12, 14–22, 26, 29–33, 35–37). These studies used a broad range of control groups and included a broad range of MTBI severity. Because of the strength of these studies and the consistency of findings, the evidence that MTBI has little short- or long-term effect on children's cognitive functioning or behavioural development can be considered persuasive. However, 2 studies report discrepant findings. One described more hyperactivity in children with MTBI, but the authors state that hyperactivity could have been present before the injury, and it may have been a causal factor for the head injury, rather than an outcome of it (11). The other reported the development of a slight visual closure deficit in young children (34). The visual closure deficit was assessed by a timed test of the child's ability to find partially concealed objects embedded in pictures. The MTBI cases and controls (having other injuries) showed no differences in performance on this test within the first month of injury, but there were differences at 6 and 12 months after the injury. Visual closure test scores were not related to reading ability when the children were again assessed at the age of 6.5 years, 2–4 years after the injury.

Most studies found no MTBI-attributable deficits in school

Table I. *Prognosis after mild traumatic brain injury (MTBI) in children*

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Anderson et al., 2000 (9)	Ages 3–12 years, admitted to neurosurgery, GCS 13–15, with altered consciousness, normal imaging and neurological exam ($n = 36$)	12 months	Prognostic factors: age, baseline functioning. Outcome: IQ	Phase I: No deficits at baseline or 1 year. Age at injury not important
Anderson et al., 2000 (10)	Cases: ages 2–7 years, admitted to neurosurgery, GCS 13–15, with altered consciousness, normal imaging and neurological exam ($n = 19$). Controls: non-injured, matched on age, gender, SES and pre-injury ability ($n = 35$)	Initial testing within 3 months, and followed at 6, 12, 18 months	Prognostic factors: MTBI presence, severity. Outcome: intelligence and memory	Phase I: No memory or intellectual deficits at baseline or follow-up
Basson et al., 1991 (37)	Hospitalized children. Cases: GCS 14–15, normal CT ($n = 40$). Control group 1: other injuries ($n = 40$). Control group 2: appendectomies ($n = 80$)	N/A	Prognostic factors: presence and type of injury. Outcome: parent-reported change in behaviour after injury	Cross-sectional: At 2 months to 5 years post-injury, injured groups had similar prevalence of behavioural disturbance, which was greater than the appendectomy patients
Bijur et al., 1990 (11)	Birth cohort, children injured between ages 5 and 10 ($n = 3182$ injuries, of which 114 were concussions, coded as ICD codes 850 or 780)	5 years	Prognostic factors: intelligence, aggression, hyperactivity, gender, social factors, mother's health, hospitalizations and other injuries Outcome: cognitive ability, hyperactivity and aggression	Phase II: No differences between head and other injuries except small difference in teacher-reported hyperactivity, which authors report could be cause or effect of injury
Bijur et al., 1996 (12)	Birth cohort. Cases: head blow requiring ambulatory care or up to 2 days in hospital ($n = 1915$). Controls: other injuries matched on gender and number of injuries ($n = 1915$)	5 years	Prognostic factors: type and number of injuries. Outcomes: cognitive tests, reading and math tests	Phase II: No differences in cognitive abilities. Cognitive deficits explained by social and personal factors, not type or number of injuries
Farmer et al., 1987 (13)	Ages 0–13 years, seen in emergency but not hospitalized. Cases: MTBI with transient altered consciousness ($n = 212$). Controls: other injuries ($n = 249$)	3 days, 2 weeks and 2 months	Prognostic factors: type of injury, age, gender, SES, LOC, vomiting, headache. Outcomes: signs and symptoms	Phase II: Children suffering minor injury have transient symptoms regardless of injury type
Fay et al., 1993, 1994 (14, 15); Jaffe et al., 1992, 1993, 1995 (18–20); Polissar et al., 1994 (29); Rivara et al., 1992, 1993, 1996 (31–33); Yorkston et al., 1997, 1999 (35, 36)	Ages 6–15 years. Cases: MTBI seen in emergency, GCS 13–15 with LOC ($n = 53$). Controls: where controls included, they were matched on classroom, age, gender, teacher-rated behaviour and academic performance ($n = 53$)	3 weeks to 3 years	Prognostic factors: MTBI injury. Outcomes: cognitive tests, parent and teacher rated behaviour, family functioning and school achievement	Phase II: No deficits in cognitive ability, school achievement, family functioning, behaviour, language, social development at any follow-up period
Fletcher et al., 1990 (16)	Ages 3–15 years, admitted to paediatric neurosurgery, MTBI ($n = 13$)	6 and 12 months	Prognostic factors: time since injury. Outcomes: behaviour and cognitive tests	Phase I: No deviation from norms at any follow-up period
Greenspan & MacKenzie, 1991 (17)	Ages 5–15 years, hospitalized for head trauma, AIS 2 or more, GCS 13–15 ($n = 60$)	1 year	Prognostic factors: head injury severity, other injuries, health, age, race, gender, parent education and family income. Outcome: health, symptoms, behaviour and special education	Phase II: MTBI not associated with poor outcome. Poverty strongly associated with poor outcome
Hahn et al., 1988; Hahn & McLone, 1993 (38, 39)	Ages 0–16 years, admitted to hospital, GCS 13–15 ($n = 791$)	To discharge. Those with seizures followed 7 years, but follow-up rate unclear.	Prognostic factors: length of LOC. Outcomes: GOS, seizure occurrence and need for neurosurgery	Descriptive: 98.65% made good recovery, 0.25% died. All with LOC <15 minutes had good outcome. 5.9% developed seizures

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Kaufmann et al., 1993 (21)	Ages 7–16 years, admitted to paediatric neurosurgery, GCS 13–15, LOC <15 minutes, no neurological deficits ($n = 11$)	6 months	Prognostic factors: none. Outcomes: cognitive tests	Phase I cohort: No persistent deficits
Kinsella et al., 1999 (22)	Ages 5–15 years, hospitalized for at least 24 hours, GCS 13–15, some LOC <20 minutes or PTA <24 hours, no focal neurological signs, normal CT ($n = 29$)	3 months, 1 year and 2 years	Prognostic factors: pre-morbid factors and injury severity. Outcome: parent and teacher report of child behaviour and family functioning	Phase II cohort: No increase in behaviour problems post-injury
Kraus et al., 1987 (23)	Population-based, children under 15 years, presenting to hospital with TBI in 1981, MTBI defined as GCS 13–15, no abnormal imaging, no need for surgery ($n = 606$)	To discharge	Prognostic factors: age, injury type, skull fracture, injury severity and neurological deficit. Outcome: death, hospital days and disabilities at discharge	Phase I cohort: 0% mortality. Median hospital stay was 1–2 days. One child had diminished visual fixation at discharge
Lazar et al., 1997 (24)	Ages 2–14 years. Cases: GCS 13–15, no neurological sequelae, discharged after 24 hours ($n = 50$). Control group 1: injured, admitted for fractures of long bones ($n = 50$). Control group 2: hernia repair ($n = 50$)	6, 12 and 24 months for cases. No follow-up of controls	Prognostic factors: injury presence and type. Outcomes: serum potassium, sodium and glucose and white blood count	Phase II cohort: Injured groups had higher glucose serum levels and white blood counts. Serum sodium and serum potassium lower in concussed patients than the other groups but normalized within 24 hours
Luerssen et al., 1988 (27)	Ages <15 years, hospital admissions, GCS 13–15 with alteration in consciousness, seizure or skull fracture ($n = 1472$)	To discharge	Prognostic factors: age Outcome: death	Phase II cohort: 0% mortality rate for GCS 13–15
Levi et al., 1991 (25)	Ages <14 years, admitted for neurosurgical evaluation and treatment, GCS 13–15 ($n = 385$)	3 months for those without good outcome at discharge	Prognostic factors: head injury severity, skull fracture and age. Outcome: GOS	Phase I cohort: 100% good recovery or mild disability
Light et al., 1998 (26)	Ages 8–16 years. Cases: MTBI, head AIS 1–3, seen in emergency ($n = 119$). Control group 1: other injuries, seen in emergency, age-matched ($n = 114$). Control group 2: uninjured school controls, age, gender and ethnicity matched ($n = 106$)	1 year	Prognostic factors: presence and type of injury. Outcomes: child behaviour checklist and academic performance	Phase II cohort: No differences in school grades or achievement scores. Injured groups had more behaviour problems than controls and lower academic scores pre- and post-injury
Ong et al., 1996 (28)	Aged <15 years admitted to neurosurgery, admission GCS 13–14 or GCS 15 if deterioration within 24 hours. Excluded those discharged at 6–12 h with normal imaging ($n = 51$)	6 months	Prognostic factors: injury severity, age, hypoxia and CT findings. Outcome: Glasgow Outcome Scale	Phase II cohort: 98% had good recovery or mild disability. One child (abnormal CT) had poor outcome
Ponsford et al., 1999 (30)	Ages 6–15, presenting at emergency. Cases: GCS 13–15, LOC <30 minutes, PTA <24 hours, no focal signs, no need for surgery ($n = 130$). Controls: other minor injuries ($n = 96$)	1 week and 3 months	Prognostic factors: type of injury, prior head injury, prior learning difficulties and prior neurological psychiatric or family problems. Outcome: symptoms, behaviour and cognitive tests	Phase II cohort: Cases had more headaches, dizziness and fatigue than controls at 1 week, no differences in cognitive findings. At 3 months, no differences between groups. Crude relationships show that cases with persistent problems had prior head injuries and more pre-morbid stressors
Wrightson et al., 1995 (34)	Ages 2.5 and 4.5 years, seen in emergency. Cases: MTBI ($n = 78$). Controls: other injuries ($n = 86$)	1 month, 6 months, 12 months, and 2–4 years	Prognostic factors: injury type. Outcome: cognitive tests, school performance	Phase II cohort: No differences at 1 month. At follow-up, the cases were worse on the visual closure test (5.47 vs 7.00 at 6 months, 6.60 vs 8.42 at 12 months, 22.44 vs 25.7 at 6.5 years. More cases in remedial reading (29% vs 14%). No other cognitive or teacher-rated differences

GCS = Glasgow Coma Scale; IQ = intelligence quotient; SES = socio-economic status; CT = computer tomography scan; N/A = no follow-up; ICD = International Classification of Diseases; LOC = loss of consciousness; AIS = Abbreviated Injury Scale; GOS = Glasgow Outcome Scale.

performance (11, 14, 15, 17–22, 26, 29, 31, 35, 36). There is 1 report that more children with a history of MTBI were enrolled in remedial reading post-injury, but no other teacher-rated deficits were reported (34). Two phase II cohort studies report that, where deficits are found in functioning, the determinants are personal and social factors, such as pre-morbid stressors and poverty, rather than the MTBI itself (12, 17).

Only 2 studies examined whether a prior head injury is a risk factor for persistent symptoms after a second MTBI. The findings are inconsistent, with 1 study which did not consider confounding suggesting a positive relationship (30), and the other study, a larger one in which the analysis adjusted for other factors, reported no relationship (12).

Two studies suggest that injured children have more post-traumatic behavioural disturbances than uninjured children, regardless of whether the injury was a head injury or another type of injury (26, 37). These findings emphasize the importance of using an appropriate comparison group when attempting to evaluate sequelae in children with head injuries. Use of an appropriate comparison group assists in differentiating any effects of a head injury from outcomes that may be due to pre-injury characteristics, extra-cranial influences or the general deleterious effects of a traumatic event.

Mortality and disability. Children's mortality after traumatic brain injury (TBI) is low, ranging from 0% (23, 25, 27, 28) to 0.25% (39). In the latter study, the fatalities were characterized by an initial Glasgow Coma Score (GCS) of 13 with deterioration after admission to hospital. The Glasgow Outcome Scale (GOS) (40) is a frequently used outcome measure for gross assessment of disability after traumatic brain injury. Scores are usually determined through an interview, usually unstructured, and classify patients into 5 categories: dead, vegetative, severely disabled (conscious but dependent), moderately disabled (independent but disabled) and good recovery (may include mild residual effects). Despite its widespread use in assessing outcome after brain injury, several limitations should be considered in interpreting the findings of studies using GOS to assess outcome after MTBI. The GOS is limited in its ability to distinguish mild disability and complete recovery, it does not consider pre-injury status in assigning a disability score, nor does it distinguish disabilities attributable to the MTBI from disabilities resulting from injuries to other parts of the body (41).

Disability (as assessed by GOS or equivalent measure) on discharge was uncommon, and in most studies, it is unclear whether the disability noted was caused by the MTBI or by other associated injuries. The overall frequency of moderate to severe disability in children with admission GCS score of 13–15 ranged from 0% to 1% (23, 25, 38). One small study ($n = 51$) of a group of more severely injured children (initial GCS 13–14 or GCS 15, deteriorating within 24 hours) reports that 2% have moderate to severe disability at 6 months (28). Only 1 of the above 4 studies (23) provides sufficient information to clearly attribute the disability to the MTBI, rather than to other associated injuries.

Neuroendocrine and metabolic response after MTBI. One study reports higher initial serum glucose levels in injured children (MTBI and other injuries), with lower serum sodium and serum potassium in the MTBI cases (24). These abnormalities resolve spontaneously within 24 hours.

Summary of prognosis after MTBI in children. There is a great deal of uniformity in the findings of the methodologically acceptable studies on the prognosis of MTBI in children. Where post-concussion symptoms are present, they are usually transient in nature, and by 2 weeks to 3 months, symptoms are similar to groups of children who have sustained other types of injuries (such as orthopaedic injuries). The evidence also suggests few short- or long-term cognitive deficits. Most of the evidence also suggests that children with MTBI do not have higher rates of subsequent behavioural or school problems than children with other types of injuries.

Prognosis of mild traumatic brain injury in adults

There were 66 accepted studies relating to prognosis of MTBI in adults, 10 of which relate to MTBI sustained in athletic events (Table II). There were 34 cohort studies, of which 18 were Phase I (42–59) and 16 were phase II studies (5, 27, 60–73). One study was a randomized controlled trial, in which a phase I analysis provides information on prognosis (74), another 1 was a systematic review (75), 10 were cross-sectional studies (76–85) and 20 (86–103) were case series or variant designs.

Cognitive sequelae. This section summarizes the evidence about cognitive sequelae after a single MTBI, as identified through formal cognitive assessments. The accepted studies provide consistent and methodologically sound evidence of cognitive deficits within the first few days after the injury, including problems of recall of material, speed of information processing and attention (42, 44, 53–56, 59, 70, 83, 84). Only 4 studies used an injured control group, and only 1 of these compared pain and distress between them, finding greater levels in the MTBI group (42). Consequently, we cannot rule out the possibility that injury-related pain and distress play a role in the observed cognitive deficits immediately after MTBI.

There are consistent findings that early cognitive deficits in MTBI are largely resolved within a few months post-injury, with most studies suggesting resolution within 3 months (44, 53, 54, 70, 79, 96). Since this evidence is based on a variety of study designs, in a number of different MTBI populations and through comparisons with both injured and non-injured control groups, we consider it persuasive and consistent evidence.

Predictors of cognitive functioning after MTBI. None of the accepted studies examining the question found an association between loss of consciousness and increased deficits in cognitive functioning after MTBI (55, 59, 80, 80, 94). However, a phase I study provides limited evidence that focal brain lesions and/or depressed skull fractures are risk factors for poorer cognitive functioning within the first 3 months after MTBI (58). It should be noted that a number of experts consider the presence of focal brain lesions or depressed skull fracture to reflect a moderate, rather than a mild brain injury (104).

Few accepted studies examined the effect of multiple concussions on cognitive ability, although cross-sectional studies

indicate that athletes who have sustained repeated head blows and concussions while playing soccer frequently show deficits in cognitive functioning (77, 81). However, no causal inferences can be made and these findings should be considered suggestive only, due to the use of a cross-sectional design. For example, the design cannot rule out the possibility that there are prior differences in players who are more likely to sustain multiple concussions. However, given the dose-response relationship found between head blows/concussions and cognitive deficits, this research question merits further attention in the form of a longitudinal study which clearly assesses the existence of an independent causal association between multiple concussions and cognitive functioning.

Self-reported symptoms and functional recovery after MTBI. This issue was examined in 7 phase II prognostic cohort studies, 5 phase I, 3 cross-sectional, and 3 case series or descriptive studies. Those injured in sports commonly experience symptoms of headache, blurred vision, dizziness, self-perceived memory problems and confusion immediately after concussion (48, 53, 55, 71). Other populations of adults with MTBI report similar physical and self-perceived cognitive symptoms after their injury, most commonly headache, fatigue, forgetfulness and sleep difficulties (42, 68, 74, 82, 89, 94, 95). These symptoms are not unique to MTBI, although they are more common within the first month after MTBI than after other injuries or in the general population (42, 68, 82). In particular, patients with non-head injured chronic pain report frequent and severe post-concussion symptoms, including substantial degrees of self-perceived cognitive deficits (92).

Findings from studies of sports-related injuries (including injuries sustained in American football and Australian football or rugby) consistently indicate resolution of symptoms within 15 minutes to 2 weeks (48, 53, 55, 71). However, where studies address other adult populations, findings on duration of symptoms after MTBI are mixed. One phase I cohort reports that symptoms after MTBI are largely resolved within 3 weeks (as assessed by self-reported absence of acute post-MTBI symptoms) (74); 1 phase II study reported resolution within 3 months (for MTBI cases not seeking compensation compared with non-injured matched controls) (67); and 1 phase I and 1 phase II study report resolution within 1 year (compared with injured controls) (47, 64). In the last 2 studies, no interim follow-up was done, so it is unclear when in that year symptoms had subsided. However, in another large study, more symptoms were reported in MTBI cases than injured controls, as long as 5 years after the injury, although some of these symptoms (pain and depression) were attributable to injuries other than MTBI (66). There was also no measure of other factors emerging during that period, such as changes in life circumstances, or health status that might confound the association between type of injury and symptoms at 5 years. Likewise, in a cross-sectional study of injuries that had occurred 1–5 years previously, MTBI cases reported more self-perceived cognitive problems than uninjured controls. Again, however, no differentiation was made between long-term sequelae specific to MTBI and sequelae possibly attributable to associated injuries, pre-morbid factors, or post-injury events (76).

Since symptoms are most often ascertained through self-report, it is important to consider the possible role of recall bias or selective differences in reporting of symptoms after MTBI. There has been little empirical study of these issues in the MTBI population, but 1 study addressed accuracy in recall of pre-injury symptoms. This study found that subjects, who had sustained a concussion an average of 6 months previously, underestimated their pre-concussion symptoms by 97% (78). This highlights the importance of using an appropriate control group, as significant recall bias may influence the internal validity of studies in which concussed subjects are asked to estimate their pre-injury symptoms, or report current symptoms as compared with pre-injury symptoms.

Summary. There is consistent evidence that adults experience symptoms, especially headache, in the acute stage and during the first month after MTBI. Although symptoms are common after MTBI, they are not unique to this type of injury since they are also evident in chronic pain patients, in other types of injuries and in healthy controls. Therefore, post-concussion symptoms should be assessed in the light of the background prevalence of these symptoms and with attention to other possible contributing factors. Few studies, for example, have adequately assessed the role of psychological distress and depression after an injury, medication effects or pain from associated injuries in the aetiology of symptoms in the acute stage of MTBI.

Prognostic factors for persistent symptoms

The stronger studies, utilizing appropriate control groups and controlling for confounding factors, suggest that post-concussion symptoms are largely resolved within 3 months to a year. However, some individuals experience persistent symptoms after MTBI, and several studies have attempted to identify reasons for this. There is evidence that some of the observed long-standing post-concussion symptoms may be attributable to factors other than the MTBI. Studies that examine the relationship between litigation and/or compensation issues and slower recovery after MTBI consistently report an association between them (5, 42, 67, 69, 75, 91, 99, 102, 103). For example, a meta-analysis of 17 studies found that financial compensation was a strong risk factor for long-term disability, symptoms and objective findings after MTBI (75). Subsequent to that meta-analysis, Paniak et al. (67, 69) found that compensation-seeking strongly predicted delayed return to work, more long-term symptoms and greater symptom severity, independent of MTBI injury severity. Amongst individuals with MTBI making insurance claims after motor vehicle collisions, the insurance compensation system (tort, compared with no-fault) was one of the strongest factors associated with slower recovery, again independent of injury severity (5). However, there is a need for further study of this issue, particularly phase III (confirmatory) studies.

Other than litigation or compensation, there is little uniformity in the identification of predictors of delayed recovery

Table II. *Prognosis after mild traumatic brain injury (MTBI) in adults**

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Bazarian et al., 1999 (42)	Cases: ER presentations; LOC <10 minutes or amnesia for event; GCS 15, no skull fracture, focal deficit or imaging abnormality ($n = 71$). Controls: orthopaedic injuries matched on IQ and socio-demographics ($n = 59$)	1, 3 and 6 months. 69 cases at 1 and 3 months, 65 at 6 months	Prognostic factors: type of injury, cognitive and psychological functioning, socio-demographics and litigation. Outcomes: PCS (DSM-IV) and symptoms	Phase I cohort: 58% of cases and 35% of controls had PCS at 1 month. Cases had baseline cognitive deficits. Litigating predicts PCS (PPV = 100%). Female gender important
Benson et al., 2002 (60)	Ice hockey players in the Canadian Inter-University Athletic Union hockey season. Population-based. Concussion defined as TBI requiring assessment or treatment by team therapist or doctor ($n = 79$)	To return to play	Prognostic factors: prior concussions, type of face shield, game or practice, position and experience level. Outcome: time lost from games or practice	Phase II cohort: Those with prior concussions lost 3.43 (95% CI 2.68–4.32) sessions if they wore half face shield and 2.43 (95% CI 1.81–3.24) session if they wore full shield. With no prior concussion, lost time was 2.09 (95% CI 1.48–2.93) with half shield and 1.0 (95% CI 0.57–1.62) with full shield
Binder & Rohling, 1996 (75)	All severities of closed head injury. 17 studies yielded 18 study groups ($n = 2353$)	None	Prognostic factor: financial incentives. Outcomes: symptoms, ratings by relatives, clinicians, return to work and cognitive variables	Meta-analysis Weighted effect size of financial incentives was 0.47 for all severities, and 0.89 for MTBI
Bohnen et al., 1994 (76)	Age 15–65. Cases: hospitalized MTBI, defined as PTA <60 minutes and LOC <20 minutes ($n = 231$). Controls: matched on medical practice attended, age and gender ($n = 231$)	None	Prognostic factors: injury type, adjusted for age, alcohol, smoking, prior health, sex and education. Outcome: symptoms	Cross-sectional: At 1–5 years post-injury, cases and controls experience the same kinds of distress but more severe for cases
Bryant & Harvey, 1998, 1999, 1999 (45, 61, 85); Harvey & Bryant, 1998 (50)	Adults 16–65 hospitalized at least 1 day after MVC. Cases: MTBI (PTA <24 hours), other injuries not excluded ($n = 79$). Controls: where used, other injuries ($n = 92$)	1 and 6 months	Prognostic factors: acute stress disorder type of injury, age, PTA, PTSD Outcomes: acute stress disorder, PTSD and post-concussion symptoms	Cross-sectional, phase I and II: ASD more frequent when prior psychiatric history. ASD is a strong predictor of PTSD. Cases and controls had similar rates of ASD and PTSD. Post-concussion symptoms more common in cases than controls and more common in cases with PTSD
Cassidy et al., 2003 (5)	Adults who made insurance claims for traffic injury, hit their head in collision, report definite or possible LOC, in hospital 2 days or less ($n = 479$)	1 year	Prognostic factors: sociodemographic, collision-related, initial symptoms, pain, prior health, healthcare provider, insurance system. Outcome: time to claim closure	Phase II cohort: Single people recovered faster. Off work after injury, not at fault, nausea or memory problems, greater % of body pain, claimed under tort system closed claims slower. Improvement in health predicted claim closure–10% improvement in physical and mental health associated with a 60% and 45% (respectively) increase in rate of claim closure
Dikmen et al., 1995 (46)	Adults, hospitalized, GCS 13–15 with any LOC or PTA >1 hour or other evidence of cerebral trauma ($n = 108$)	1 year	Prognostic factors: blood alcohol level in ER, prior drinking patterns Outcome: alcohol consumption	Phase I cohort: Blood alcohol levels at ER indicate problem drinking. Those with MTBI decrease drinking after injury but less than severe injuries

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Dikmen et al., 1995 (47)	Cases: adults, hospitalized, any LOC or PTA >1 hour, able to follow commands less than 1 hour from injury ($n = 161$). Controls: other injuries, ($n = 121$)	1 year	Prognostic Factors: type of injury. Outcome: cognitive functioning	Phase I cohort: No cognitive test deficits at 1 year
Ferguson et al., 1999 (78)	Cases: athletes with sports concussion (PTA <24 hours) within past year ($n = 50$). Controls: athletes without head injuries ($n = 159$)	None	Prognostic factors: concussion. Outcomes: symptoms before and after injury (cases), current symptoms and symptoms expected if concussed (controls)	Cross-sectional: At 6 months post-injury, cases reported same current symptoms as controls but underestimated prior symptoms by 97%
Friedland & Dawson, 2001 (62)	Adults with motor vehicle injuries, admitted to tertiary care centre, excluded if very serious associated injuries. Cases: GCS 13–15, LOC <30 min, PTA <24 hours ($n = 64$). Controls: other injuries ($n = 64$)	6 and 9 months	Prognostic factors: type of injury, posttraumatic stress, demographic characteristics. Outcome: functional recovery and return to work	Phase II cohort: Functional recovery same for cases and controls. Cases were more distressed. Post-traumatic stress predicted slower recovery
Garraway & MacLeod, 1995 (48)	Rugby players with sports concussion ($n = 20$)	To return to play, work or school	Prognostic factors: none. Outcomes: days to return to activities	Phase I cohort: Average of 22.5 (SD 3.5) days of lost play; 55% had school or work absence, which averaged 3.5 (SD 0.6) days
Gennarelli et al., 1994 (63)	Trauma patients of all ages, admitted to trauma centre ($n = 174{,}160$). Cases: MTBI ($n = 46{,}977$). Controls: other injuries	To discharge	Prognostic factors: type of injury, AIS, mechanism of injury. Outcome: mortality and disability	Phase II cohort: For AIS 1 and motor vehicle injuries, 0% mortality for cases, 0.6% for controls. For AIS 1 and non-motor vehicle injuries, 0% mortality for cases and 1.1% for controls. No increased disability at discharge for cases
Gentilini et al., 1985 (79)	Cases: ages 13–75, GCS 13–15, LOC <20 minutes, normal neurological exam, hospitalized less than 3 days ($n = 50$). Controls: spouse, friend, relative, schoolmate of cases ($n = 50$)	None	Prognostic factors: none. Outcomes: cognitive tests	Cross-sectional: No differences at 1 month
Greiffenstein & Baker, 2001 (49)	Adults making claims or litigating for late PCS syndrome, referred for assessment, 22 of 23 subjects had GCS 12–15, 4 subjects had sustained whiplash, 15 subjects had no altered consciousness, and 3 subjects had <1 hour PTA. All had a pre-injury MMPI administered for other reasons	MMPI administered 1–16 years after TBI, mean of 6.3 years	Prognostic factors: none. Outcome: changes in MMPI profile	Phase I cohort: Post-injury MMPI abnormalities may reflect pre-morbid personality
Hanks et al., 1999 (64)	Adults 15–83 years, admitted to level 1 trauma centre, GCS 13–15 with LOC, PTA >1 hour or other evidence of brain trauma ($n = 138$). Controls: other injuries, not brain injuries ($n = 125$), community controls ($n = 450$)	1 year	Prognostic factors: presence, type of injury Outcomes: Katz Adjustment Scale	Phase II cohort: No differences in emotional or behavioural adjustment between cases and injured controls. Both injured groups had poorer adjustment than uninjured controls

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Hsiang et al., 1997 (51)	Age 11 years and over, admitted to neurosurgery (Hong Kong), GCS 13–15 ($n = 1360$)	6 months	Prognostic factors: GCS and radiological abnormalities. Outcomes: Glasgow Outcome Scale	Phase I cohort: Good outcome in 98% of GCS 15, 93% of GCS 14, and 76% of GCS 13. Good outcome in 89% of those with GCS 13–14 or radiographic abnormalities. Poor outcome in GCS 15 with normal radiography was due to other factors
Iverson et al., 2000 (80)	Adults admitted to trauma hospital with GCS 13–15 with altered consciousness, normal imaging and no neurological deficits ($n = 195$)	None	Prognostic factors: LOC present, absent or equivocal Outcomes: acute cognitive functioning	Cross-sectional: Within 1 week, no differences between groups on most tests. Equivocal LOC had worse scores on Trails B than positive or negative LOC groups (no explanation given)
Kraus & Fife, 1985 (52)	Men, aged 16 years and over, admitted to hospital, GCS 13–15, work-related injuries. ($n = 84$)	To discharge	Prognostic factors: none. Outcomes: Glasgow Outcome Scale.	Phase I cohort: 100% discharged with good recovery
Kraus et al., 1989 (65)	Hospitalized, MTBI defined as GCS 13–15, normal CT, no need for surgery, over age 14 years (n of all TBI = 2649)	To discharge or death	Prognostic factors: blood alcohol level. Outcomes: neurological limitations at discharge	Phase II cohort: Systematic bias in obtaining blood alcohol levels precludes determining relationship between blood alcohol and outcome
Lovell et al., 1999 (59)	Admitted to trauma centre, GCS 14–15, no skull fracture or intracranial abnormality ($n = 383$)	Up to 7 days	Prognostic factors: certain, uncertain or no LOC. Outcomes: cognitive testing	Phase I cohort: Mild deficits in speed of information processing, attention and memory but not related to LOC
Lowden et al., 1989 (74)	Presenting to ER with LOC or amnesia for event, with PTA <15 minutes; excludes other injuries requiring admission, skull fracture, neurological signs ($n = 111$)	6 weeks	Prognostic factors: none Outcomes: symptom presence and duration	RCT. Prognostic analysis was Phase I: 90% had symptoms. Median length of symptoms was 1 week (95% CI 1–3 weeks), with headaches lasting longest
Luerssen et al., 1988 (27)	Ages up to 90 years, hospitalized, GCS 13–15 with altered consciousness, seizure or skull fracture ($n = 5883$)	To discharge	Prognostic factors: age Outcome: death	Phase II cohort: 0.9% mortality in ages over 14 years, cause of death not reported
Macciocchi et al., 1996 (53)	Cases: football players, concussion with LOC up to 5 minutes ($n = 183$). Controls: matched students ($n = 48$)	1, 5, 10 days, 12 weeks	Prognostic factors: concussion. Outcomes: cognitive tests and symptoms (for cases)	Phase I cohort: Cases had initial test deficits. At 10 days, no differences in tests, no headaches, but some dizziness and self-reported memory problems in cases
Maddocks & Saling, 1996 (54)	Cases: Australian Rules Football players, sports concussion ($n = 10$). Controls: age and education matched umpires ($n = 10$)	5 days	Prognostic factors: concussion and pre-injury test scores (for cases). Outcomes: symptoms and cognitive tests	Phase I cohort: Headache and nausea had resolved at 5 days but cases had mild cognitive deficits
Masson et al., 1996 (66)	Age 15 years and up, admitted to hospital. Cases: GCS 13–15, no abnormal imaging, excluded those with other injuries with AIS >2 ($n = 119$ at follow-up). Controls: lower limb injuries ($n = 64$ at follow-up)	5 years	Prognostic factors: injury type. Outcomes: symptoms, Glasgow Outcome Scale	Phase II cohort: At 5 years, cases had more headaches (44 vs 16%), also more memory problems, dizziness, sleep disturbance, depression, anxiety, irritability, and less pain. Pain and depression in cases was associated with other injuries. No difference in disability. Poor recovery in cases not due to MTBI
Matser et al., 1999 (81)	Cases: 3 teams of amateur soccer players ($n = 33$). Controls: runners and swimmers ($n = 27$). Concussions self-reported	N/A	Prognostic factors: athlete engaging in sport with or without head blows. Outcomes: cognitive tests	Cross-sectional: Cases had impaired planning and memory

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Matser et al., 2001 (77)	Professional soccer players (volunteers). Players had median 500 headers (10 th percentile = 70; 90th percentile = 1,260) headers in a season and a median of 1 concussion (90th percentile was 12) during career ($n = 84$)	None	Prognostic factors: number of headers, concussions, adjusted for age, education, alcohol, history of general anaesthesia, non-soccer concussions. Outcome: cognitive tests	Cross-sectional: Number of headers was associated with deficits in focused attention and visual/verbal memory, number of soccer-related concussions associated with deficits in sustained attention and visuoperceptual processing
McCrory et al., 2000 (55)	Australian Rules football players with concussion, defined as transient altered consciousness or disturbance of vision or equilibrium ($n = 23$)	15 minutes post-injury and to return to play	Prognostic factors: pre-injury scores. Outcomes: number, type and duration of symptoms and Digit Symbol Substitution Test	Phase I cohort: 100% had headaches (40% of these lasted longer than 15 minutes). Slowed Digit Substitution test at 15 minutes. 43% returned to play same day and all returned within 2 weeks
McMillan & Glucksman, 1987 (56)	Admissions to hospital. Cases: MTBI with LOC and PTA 1–24 hours ($n = 24$). Controls: adults with orthopaedic injuries ($n = 24$)	Follow-up after discharge for up to 7 days	Prognostic factors: type of injury. Outcome: cognitive tests and symptoms	Phase I cohort: MTBI cases showed impaired information processing speed and self-perceived memory deficits
Ommaya et al., 1996 (43)	Persons discharged from US Military. Cases: had been hospitalized with MTBI, defined as head AIS 1–2 ($n = 1778$). Controls: all discharged personnel ($n = 1,877,946$)	To discharge from forces or up to 2.7 years	Prognostic factors: none. Outcomes: reason for discharge	Phase I cohort: For cases, discharge due to alcohol/drugs OR (95% CI) = 2.6 (1.6–4.3); for behaviour problems OR = 1.8 (1.4–2.2), criminal conviction OR = 2.7 (1.9–3.9), medical disability OR = 7.5 (6.0–24.0), death (not necessarily due to head injury) OR = 13.5 (7.7–24.0)
Paniak et al., 2002 (67)	Cases: presentations to ER, GCS 13–15, LOC <30 minutes, PTA <24 hours ($n = 68$). Controls: volunteers matched on age, sex, education and SES ($n = 118$)	3 and 12 months	Prognostic factors: compensation seeking, SES, ISS (non-brain injuries), treatment satisfaction, age, gender, ethnicity, head injury severity, medication use and prior psychological treatment. Outcomes: presence and severity of symptoms	Phase II cohort: Demographics and injury severity did not predict compensation seeking. Compensation seeking predicted more symptoms. Effect size 0.88 at baseline, 1.03 at 3 months and 0.96 at 1 year. No difference in symptoms between cases not seeking compensation and controls
Paniak et al., 2002 (68)	Cases: presentations to ER, GCS 13–15, LOC <30 minutes, PTA <24 hours ($n = 118$). Controls: volunteers matched on age, sex, education and SES ($n = 118$)	Within 1 month (mean = 13 days)	Prognostic factors: MTBI, gender, age, education and SES. Outcomes: presence of symptoms and severity (on 7 point severity scale)	Phase II cohort: Cases averaged 18.7 symptoms (severity = 1.7) and controls 12.6 symptoms (severity = 0.8). No relationship between symptoms and gender, age or education
Paniak et al., 1999 (82)	Cases: presentations to ER, GCS 13–15, LOC <30 minutes, PTA <24 hours ($n = 120$). Controls: volunteers, matched to cases by age, gender, education and SES ($n = 120$)	None	Prognostic factors: MTBI. Outcomes: self-reported problems (Problem Check List), health (SF-36), and community functioning (Community Integration Questionnaire)	Cross-sectional: At 3 weeks, cases had more problems, poorer health. Physical functioning (from SF-36) had largest effect size of 3.5
Paniak et al., 2000 (69)	Presentations to ER, GCS 13–15, LOC <30 minutes, PTA <24 hours ($n = 118$)	3 months	Prognostic factors: age, gender, injury severity, alcohol use, prior health and life events, medication use, SES and financial compensation. Outcomes: return to pre-injury vocational status	Phase II cohort: Best predictor of return to work was seeking or receiving financial compensation

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Ponsford et al., 2000 (70)	Presentations to ER. Cases: GCS 13–15, LOC <30 minutes, PTA <24 hours, no focal neurological signs, no need for surgery ($n = 136$) Controls: minor other injuries not requiring surgery ($n = 71$)	3 months	Prognostic factors: type of injury, sociodemographic, and pre-morbid characteristics. Outcomes: cognitive and behavioural or psychological functioning	Phase II cohort: At 1 week, cases had more symptoms and slowed informational processing. At 3 months, symptoms had resolved in most and no differences in cognitive functioning. Continued problems in cases unrelated to MTBI severity, but related to prior head injury, prior health or psychiatric problems, life stressors, being students, female and injured in MVC
Richardson & Snape, 1984 (83)	Men, admitted to hospital after injury, aged 16–64 years. Cases: MTBI. $n = 16$ cases had coma <10 minutes. $n = 22$ cases had PTA <24 hours. Controls: orthopaedic injuries, matched on age and gender ($n = 60$)	None	Prognostic factors: type of injury. Outcomes: free recall of abstract and concrete words	Cross-sectional: At 24 hours after resolution of PTA, cases showed deficit in recall of concrete material
Richardson & Barry, 1985 (84)	Men age 16–64 years, admitted to hospital after injury. Cases: MTBI with PTA <7 hours. Those on medications at time of testing excluded ($n = 18$). Controls: orthopaedic injuries, similar to cases on age, SES and injury/testing interval ($n = 48$)	None	Prognostic factors: type of injury. Outcomes: recognition memory for faces, free oral recall of visual stimuli, free recall of concrete and abstract words	Cross-sectional: At 24 hours after resolution of PTA, no differences in recognition memory or recall of visual stimuli, but deficit in memory of words when imagery instructions not provided. Suggests that in the acute phase, MTBI patients do not spontaneously use imagery to improve recall of verbal material
Riemann & Gukiewicz, 2000 (71)	Cases: university athletes aged 18–24 years suffering mild sports concussion with GCS 13–15, LOC <15 minutes, no neurological deficits ($n = 16$). Controls: uninjured athletes, matched on age, gender, height and weight ($n = 16$)	1, 3 and 5 days	Prognostic factor: concussion. Outcomes: symptoms (cases only) and balance	Phase II cohort: By day 3, most symptoms had resolved and by day 5, only 2 cases had any symptoms. Postural instabilities present at first but have resolved by day 5
Selladurai et al., 1997 (72)	Admissions to neurosurgery after TBI, GCS <15 or GCS 15 with positive CT findings, GCS 13–15 ($n = 43$)	6 months	Prognostic factors: age, GCS, pupil reactivity, hypoxia, hypotension, CT abnormalities and haemostatic parameters. Outcome: Glasgow Outcome Scale	Phase II cohort: 42% had abnormal haemostatic parameters. 25% had poor outcome at 6 months. Outcome predicted by baseline fibrin degradation product levels
Teasdale & Engberg, 1997 (44)	Population-based. Danish men in archive of Danish draft board. Cases: hospitalized with concussion (ICD code 850) as sole diagnosis ($n = 1220$)	3 to >200 days	Prognostic factors: time between injury and testing. Outcome: cognitive test scores	Phase I cohort: Increased risk of cognitive deficits at 3–6 days (RR = 2.45, 95% CI 1.23–4.9); no increased risk up to 100 days; after 100 days, RR = 1.30 (0.87–1.93) and after 200 days, RR = 1.19, 95% CI 1.02–1.38
Teasdale & Engberg, 2000 (57)	Danish population, admitted to hospital, head injury discharge diagnosis ICD codes 850, 800, 801, 803, 851–854 ($n = 86{,}991$). Concussion defined as ICD code 850	Up to 24 years	Prognostic factors: MTBI, age, gender and grounds for disability. Outcome: disability pension award	Phase I cohort: Awarding of disability after concussion was related to risk factors for concussion rather than to concussion itself

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Thornhill et al., 2000 (73)	Glasgow residents aged 14 years or older, hospitalized for head injury (507 had GCS 13–15 and 362 of these were followed)	1 year	Prognostic factors: age, gender, cause of injury, pre-existing physical limitations and history of brain illness. Outcome: Extended Glasgow Outcome Scale, problems in daily living and employment status	Phase II cohort: 47% had moderate/ severe disability and sequelae, which had been previously unrecognized. Age over 40 years, pre-existing physical limitations and history of brain illness were predictors of poor outcome
Williams et al., 1990 (58)	Ages 16–40 years, admitted to neurosurgery. Mild TBI defined as GCS 13–15, normal CT, may include linear or basilar skull fracture. Mild complicated TBI defined as GCS 13–15 with focal brain lesion, depressed skull fracture or both (n = 215 with 23% to 48% loss to follow-up for cognitive testing)	1–3 months for cognitive testing, 6 months for Glasgow Outcome Scale	Prognostic factors: MTBI complications. Outcomes: cognitive tests, Glasgow Outcome scale	Phase I cohort: Mild better than mild complicated on mean verbal fluency (35.35, SD 28.26 vs 23.61, SD 22.36), information-processing rate (0.56, SD 0.24 vs 0.41, SD 0.19) and recognition memory (86.50, SD 7.51 vs 80.55, SD 12.37). 97.10% MTBI without and 83.78% with complications had good recovery

*Some case series or descriptive studies (41, 86–103, 105) are not included in table due to space considerations.
ER = emergency room; LOC = loss of consciousness; GCS = Glasgow Coma Scale; IQ = intelligence quotient; PCS = post-concussion syndrome; DSM-IV = Diagnostic and Statistical Manual Version IV; PPV = positive predictive value; PTA = post-traumatic amnesia; MVC = motor vehicle collision; PTSD = post-traumatic stress disorder: ASD = acute stress disorder; ER = emergency room; SD = standard deviation; AIS = abbreviated injury score; MMPI = Minnesota Multiphasic Personality Inventory; N/A = not applicable; OR = odds ratio; CI = confidence interval; SES = socioeconomic status; ISS = injury severity score; SF-36 = the Short-Form 36 Health Survey questionnaire; CT = computer tomography; ICD = the International Classification of Diseases; RR = relative risk.

after MTBI, since there is little consistency in predictors being studied and no confirmatory studies in this area. This makes comparisons between studies difficult and inconsistencies difficult to interpret. Some studies identify female gender as a predictor of persistent symptoms (42, 70), but others found no independent relationship (5, 73). In a study of motor vehicle injury insurance claimants with MTBI, being married, being off work due to the injury, not being at fault for the collision, post-injury symptoms of nausea or memory problems and other injuries (percentage of body in pain after the collision) were independently associated with slower recovery (5). History of pre-existing physical limitations (73), prior brain illness or neurological problems (70, 73), prior head injuries, psychiatric problems, life stressors, being a student, sustaining MTBI in a motor vehicle collision (70) and age over 40 years (73) have also been identified as predictors of prolonged symptoms. Severity of the MTBI itself was not an independent predictor of persistent, long-term symptoms in any study. However, there is a report of concussed ice hockey players with prior concussions missing an average of 1–2 more games or practices than those with no prior history of concussion (60). It is unclear whether the delay in returning to play was because the injury was more severe, because it took longer for symptoms to resolve or because the history of concussion lead to increased caution on the part of the team physician in approving the return to play.

It is difficult to study the question of whether pre-morbid personality is an important predictor of persistent symptoms after MTBI. One study that addresses this issue in a unique and highly selected sample of individuals who had been administered psychological tests prior to their injury, found that post-MTBI psychological problems reflected pre-morbid personality, rather than the effects of the injury (49). This study is suggestive, but should be considered a preliminary step in the investigation of this question.

Several reports from 1 cohort of subjects examined the role of acute stress disorder and post-traumatic stress disorder in the outcome of individuals with MTBI associated with a motor vehicle injury. They show that prior psychiatric history is a risk factor for acute stress disorder following a motor vehicle collision, whether the injury included MTBI or not. In addition, acute stress disorder was a strong predictor of later development of post-traumatic stress disorder, which was, in turn, associated with more self-reported symptoms (45, 50, 61, 85). Acute post-traumatic stress after a traffic injury was also associated with delays in functional measures of recovery, such as return to work (62).

Mortality and disability

Eleven accepted studies report mortality, GOS scores, or some other measure of disability as a primary outcome. Mortality after MTBI is rare, with rates from 0% to 0.9% (27, 63, 88). However, none of these studies specify how many deaths were directly related to the MTBI vs other injuries sustained in the event.

Most studies utilizing the GOS found that patients with MTBI have a good outcome (as defined by the scale), in both the short

and the long-term (51, 52, 63, 66, 97). One study reported good outcome in 100% of all hospitalized patients with MTBI (52) and another reported 98% good outcome for GCS 15, 93% for GCS 14 and 76% for GCS 13 (51). In that study, poor outcome in GCS 15 with normal radiographic findings was rare (0.2%) and was due to factors other than the MTBI. Two studies compared outcome in injured individuals with MTBI and controls with other injuries judged to be similar in severity. They both report no differences in rates of disability (63, 66), and both conclude that the poor outcome in the MTBI cases was not due to TBI itself. Similarly, where disability pensions were awarded after MTBI, the pension was granted because of problems that are risk factors for MTBI, such as alcoholism, rather than because of the MTBI itself (57). Behavioural problems, alcohol/drug use and criminal convictions are more frequently cited as reasons for discharge from the US military in those with a history of MTBI (43). However, these reasons for discharge cannot be attributed to the MTBI, because they are also risk factors for experiencing head injuries. Similarly, the other studies that report disability after MTBI do not distinguish whether the disabilities are attributable to the MTBI, to pre-existing conditions, or to other injuries sustained in the event.

Most studies suggest a generally good outcome (little or no disability) for individuals with MTBI. However, 1 notable study suggests a much more negative prognosis. Thornhill et al. (73) followed 362 Glasgow residents aged 14 years or older, who had been admitted to hospital with MTBI. At 1 year, 47% had moderate or severe disability, according to the Extended Glasgow Outcome Scale (GOSE). They found that age over 40 years, pre-existing physical limitations and history of brain illness (e.g. stroke) were associated with poor outcome. However, the high frequency of pre-existing and concurrent co-morbid health conditions may result in questionable generalizability of these findings to other populations. In addition, since there was no follow-up prior to 1 year post-injury, it is unclear whether other events may have occurred which influenced the outcome.

Prognostic factors for disability. A small study provides some evidence that disseminated intravascular coagulation immediately after MTBI predicts poor score on the GOS at 6 months (72). Patients with GCS 13 at admission have higher rates of disability than GCS 15 (51), however, again, it is not clear how much disability is attributable to the MTBI or to other injuries.

Outcome and prognostic factors in specific subgroups of patients with MTBI

Some studies examined outcome in particular subgroups of MTBI cases.

Alcohol use. It is clear that alcohol is an important risk factor for injury occurrence. However, the role of alcohol as a predictor of poor prognosis is an under-studied area, and no conclusions can be drawn on its importance. Only 1 study specifically examined this question in a systematic manner, and concluded that blood alcohol level testing was performed too selectively to accurately determine the relationship between blood alcohol and outcome at discharge (65). Alcoholism is likely to be associated with markers of poor outcome, even in the absence of injury. However, a high blood alcohol level at presentation to emergency departments after a head injury appears to be a marker for a history of problem drinking (46). Clearly, the question of whether alcohol use is a determinant of outcome after MTBI deserves further study.

Complicated MTBI. There is some evidence from a phase I study that there is a lower rate of good recovery as assessed by the GOS when MTBI is complicated by a focal brain lesion and/or depressed skull fracture, than when such complications are not present (58). A descriptive study reports that adults with initial GCS 15, who required surgery after developing acute intracranial haematoma, are at risk for poorer outcome than those not requiring surgery (only 65% in the former group had good outcome), and there was a suggestion that delays in diagnosis in this group are also associated with poor outcome (98). While these results are not surprising, there is still a need for good studies of these patients.

MTBI in elderly people. The effect of older age on recovery from MTBI has not received much research attention. There were several case series or descriptive studies that suggest that elderly people have poorer recovery after MTBI (86, 100, 101). Unfortunately, none of these studies report information that would permit us to distinguish disabilities due to the head injury vs other injuries.

MTBI and severe associated injuries. The role of severe associated injuries in recovery from MTBI has not been well studied. One series of patients hospitalized for MTBI with severe associated injuries suggests poor outcome (only 62% had good outcome at 4–5 years post-injury). However, it was unclear whether these residual disabilities were attributable to the head injury (90).

MTBI with associated seizures. One large descriptive study explored the prognosis for adults who developed seizures after MTBI, and reported that 7% required intracranial surgery, but that 92% had good recovery at 6 months (93).

Summary. In general, the studies examining prognosis of MTBI in adults make less use of control groups than the studies of children. Where controls are used, they are usually uninjured controls, often volunteers, who may be matched on socio-demographic factors, but may be dissimilar on pre-injury symptoms or personality characteristics. Injured controls are rarely used, and the possible contributions of psychological distress or pain associated with other (non-brain) injuries have not been adequately considered.

Measures used to assess prognosis in MTBI

No separate literature search was performed to assess the reliability and validity of tests or questionnaires used to assess prognosis of MTBI, however a number of such studies were identified in the course of our search. Many of the common measurement tools have not been validated on an MTBI population. Of the studies we identified in our search that

specifically assessed the ability of these measurement tools to accurately reflect prognosis of MTBI, 4 were accepted. Two of these studies confirm the reliability of the Rivermead Post-Concussion Symptoms Questionnaire and the Rivermead Head Injury Follow-up Questionnaire (87, 105) and 1 study confirms the reliability (inter-observer agreement) of the GOSE (41). The fourth study supported the ability of the Problem Checklist (106) and the SF-36 (107), but not the Community Integration Questionnaire (108), to distinguish MTBI cases from normal controls (82).

Poor outcome after MTBI

Two widely used sets of diagnostic guidelines, the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-IV) and the International Classification of Diseases (ICD-10) provide possible criteria for diagnosing what might be referred to as poor outcome after MTBI (109, 110). The DSM-IV has proposed Postconcussional Disorder as a diagnostic category, but states that further research is required to determine the utility of the category and to study the criteria suggested. Proposed criteria for Postconcussional Disorder include a history of head trauma causing loss of consciousness (LOC) of more than 5 minutes, post-traumatic amnesia (PTA) lasting longer than 12 hours or onset of seizures within 6 months. The proposed diagnosis also specifies evidence from cognitive assessments of attention or memory deficits, 3 or more symptoms lasting at least 3 months, and resulting significant impairment in social or occupational functioning. Furthermore, Postconcussional Disorder must be distinguished from Factitious Disorder or Malingering.

ICD-10 criteria indicate that Postconcussional Syndrome occurs following head trauma, usually severe enough to result in LOC. Further criteria include a number of disparate symptoms such as headaches, dizziness, fatigue and difficult concentrating. It acknowledges that the aetiology of the symptoms is not always clear, and that both organic and psychological factors have been proposed to account for them. At least 3 of these features should be present for a definite diagnosis.

In comparing these 2 sets of criteria, there are similarities, although the DSM-IV research criteria appear to be clearer and easier to operationalize than the ICD-10 diagnostic criteria. However, the research reviewed earlier does not support the importance of injury severity threshold proposed in either the DSM-IV criteria (more than 5 minutes LOC or PTA of more than 12 hours) or the ICD-10 criteria (head trauma usually sufficient to result in LOC). We also found no evidence that length of PTA or onset of seizures after MTBI are prognostic of slower recovery or prolonged symptoms. Therefore there is little evidence-based justification in the literature for setting a particular threshold of injury severity in the diagnosis of this disorder.

There is some justification for considering a threshold of 3 months to reflect prolonged recovery, especially for children. The research reviewed earlier in this document indicates that symptoms in children are largely resolved within 2–3 months of the injury, and the great majority of paediatric MTBI studies report no short- or long-term cognitive problems or post-injury behavioural deficits attributable to MTBI. The literature on recovery time is less clear for adults, and although there is support for the idea that most adults recover within 3 months, this needs further study.

The most serious problem in the diagnosis of Postconcussional Disorder or Postconcussional Syndrome is linking residual symptoms to the MTBI. The ICD-10 criteria explicitly recognize that the cause of subjectively reported symptoms is not always clear. Nor, as noted previously in this paper, are these symptoms specific to MTBI. The most consistent predictors of delayed recovery after MTBI are compensation and litigation factors, independent of MTBI injury severity. However, it should not be assumed that all patients pursuing a compensation claim or litigation are experiencing a delayed recovery; that these factors are the only predictors of prolonged symptoms; or that settling a claim will result in quick recovery. The mechanisms through which compensation/litigation issues impact on rate of recovery are not well studied or understood.

Malingering or incomplete effort in poor outcome of MTBI. The DSM-IV diagnostic criteria require differentiation of Postconcussional Disorder from malingering, although the ICD-10 diagnostic criteria for Postconcussional Syndrome do not. Malingering is described by the DSM-IV as a condition in which desire for compensation leads to the production or prolongation of symptoms. Although, according to this description, seeking financial compensation or litigation after MTBI is a necessary condition for malingering, it should not be assumed that all or most individuals seeking compensation after MTBI are malingering.

We accepted 11 studies relating to what is frequently referred to in the literature as possible/probable malingering or incomplete effort (111–121) (Table III). Seven of these identified measures that might be useful in identifying possible or probable malingering (112–115, 118, 119, 121). However, few of these tests have yet been extensively researched, and further work is needed to cross-validate them in other samples, and to investigate their accuracy.

Seven studies report that persons with MTBI who are seeking compensation or litigating, and who are considered possible or probable malingerers, perform as badly or worse on cognitive or motor tests than do individuals with more severe brain injuries (111, 113, 115–118, 120). One of these studies (117) reports that external verbal motivation to perform well leads persons with chronic complaints after MTBI to improve their vigilance and attention test scores from the level of the severe brain injury survivor up to the level of normal controls.

However, all studies relating to malingering or incomplete effort were cross-sectional in design, and studies were performed many months or years after the injury. The studies provide no information about the frequency of malingering after MTBI, or the frequency of malingering in individuals seeking compensation or litigating. Nor can causal directions be ascertained from the current literature.

Table III. *Malingering or incomplete effort after mild traumatic brain injury (MTBI)**

Authors	Setting and subjects	Time since injury	Prognostic factors/outcomes	Design and findings
Binder et al., 1993 (113)	Referrals for neuropsychological assessment. Cases: adults with MTBI, GCS 13–15, LOC <20 minutes, no focal deficits, normal imaging at initial assessment, seeking compensation ($n = 75$). Controls: brain dysfunction with documented neurological abnormalities ($n = 80$)	Cases: average of 2 years Controls: not stated	Prognostic factors: seeking compensation, score on motivation test (Portland Digit Recognition Test). Outcome: score on Rey Auditory Verbal Learning Test	Cross-sectional: Cases had poorer motivation. 27% of cases and 5% of controls scored worse than chance. Cases with poor motivation scores had very poor scores on outcome (effect size of difference on recognition scores was 0.99)
Greiffenstein et al., 1996 (116)	Source of subjects not reported. Cases: adults with history of MTBI, PTA <1 hour; 3 or more cognitive or emotional complaints lasting at least 1 year; perceived disability at work, school or homemaking; had undergone cognitive remediation; normal physical and neurological examinations; deficient scores on motor skills portion of neuropsychological battery ($n = 131$). All seeking or receiving compensation or pursuing litigation. Controls: moderate to severe TBI; unambiguous motor abnormalities on neurological exam ($n = 54$)	Cases: average of 24 months Controls: average of 42 months (women) and 60 months (men)	Prognostic factors: TBI severity, psychological distress (MMPI-2) and pain. Outcomes: motor skills	Cross-sectional: Both groups showed motor skill deficits. The controls had deficits consistent with upper motor neurone disease. The cases had a non-physiological pattern, which was not associated with pain or emotional distress. Motor deficits in the compensation seeking MTBI patients are likely functional.
Keller et al., 2000 (117)	Tertiary inpatient rehabilitation unit. Cases: MTBI with GCS 13–15, no LOC or up to a few minutes, no neurological signs or abnormal imaging at initial assessment, chronic post-concussion symptoms ($n = 12$, 11 also had whiplash). Controls: clinic staff ($n = 11$); moderate to severe TBI patients ($n = 10$)	Cases: average of 38 months. Controls: N/A for the clinic staff and 5.5 months for the brain injured controls	Prognostic factors: presence and severity of injury, verbal motivation (experimental intervention). Outcome: scores on vigilance and attention test (Wiener D test)	Cross-sectional: Intervention of external motivation improved cases' performance from similar to severe TBI before intervention to no deficits compared to controls after intervention
Suhr et al., 1997 (120)	Tertiary referrals for neuropsychological assessment. Group 1: MTBI with no or brief LOC (average 0.3 minutes), GCS 15, litigating or seeking compensation, 2 or more of the following: total disability, contradiction between self-reported symptoms and collateral sources, reports of remote memory loss or other symptoms inconsistent with MTBI, poor performance on a symptom validity test ($n = 31$). Group 2: MTBI, average 9.5 minutes LOC, average GCS 13.8, litigating or seeking compensation but none of the above signs of malingering ($n = 30$). Group 3: mild to moderate head TBI, GCS 9 or greater, average LOC 3 hours, PTA 21 hours, not litigating or seeking compensation ($n = 20$). Group 4: Severe TBI, not litigating or seeking compensation ($n = 15$). Group 5: uninjured patients complaining of cognitive complaints and diagnosed with somatoform disorder ($n = 29$). Group 6: uninjured patients with cognitive complaints and diagnosed with depression ($n = 30$)	Average of 30 to 52 months for injured groups	Prognostic factors: malingering, compensation seeking or litigating, head injury severity, medication use, psychological status (MMPI-2). Outcome: tests of attention and verbal memory and visual memory	Cross-sectional: Probable malingerers worse on all cognitive measures. Malingering, poor psychological status and medication use were associated with poorer cognitive scores. Those seeking compensation/litigation had similar attention and memory as the more seriously injured groups

*Some studies of measures to assess malingering (111, 112, 114, 115, 118, 119, 121) are not included in the table due to space considerations. GCS = Glasgow Coma Scale; LOC = loss of consciousness; PTA = post-traumatic amnesia; TBI = traumatic brain injury; MMPI-2 = Minnesota Multiphasic Personality Inventory-2; N/A means the study did not address risk factors or did not provide explicit results for MTBI.

Summary. Neither the DSM-IV category of Postconcussional Disorder nor the ICD-10 category of Postconcussional Syndrome is strongly supported by the best available evidence. The proposed injury severity thresholds are not supported by most of the available research and the symptoms listed under each diagnosis are not specific to MTBI, thus making it difficult to link the presence of symptoms to the MTBI. There is some evidence, which is especially convincing in paediatric cases, to support the 3-month threshold proposed by the DSM-IV to reflect the time period during which most MTBI cases have recovered. However, the best studies on children with MTBI show little or no evidence of persistent problems suggestive of this disorder. In adults, the most consistent correlates of delays in recovery after MTBI relate to compensation/litigation factors and related motivational issues. This means that where there are prolonged and significant complaints after MTBI, it is important to investigate thoroughly other factors that may be contributing to the problems. The use of terms such as "Postconcussional Disorder" or "Postconcussional Syndrome" to describe long-term bad outcomes after MTBI may be misleading because of the implication that these problems are a result of the MTBI or concussion.

Is MTBI a risk factor for development of seizures/seizure disorder?

Two large population-based cohort studies examined whether MTBI is a risk factor for development of seizure disorders (122, 123) (Table IV). The second of these studies extends the findings of the first by including all subjects from the first study, and extends both the inception and follow-up periods. Therefore, findings from the later report are more informative. MTBI was found to increase the risk of seizures by 50%, primarily during the first 4 years after the injury. However, the absolute risk of seizure after MTBI remains low, and the 5-year cumulative incidence of seizure activity after MTBI is 0.7%. Neither age nor gender affected the risk of seizure activity. A much smaller, descriptive study reported that 5.9% of children hospitalized with MTBI had seizures after their injury, usually within the first 24 hours, but no information is available on how many children continued to have seizures after discharge (38, 39).

Is MTBI a risk factor for dementia?

Three studies, 2 cohort studies and 1 case-control study, addressed this issue (Table IV). Given the small number of exposed cases in the case-control study and the infrequency of dementia cases in the cohort studies, statistical precision is problematic for all 3, and results are inconsistent. Overall, the larger study concludes that head injuries are not a risk factor (124) and the 2 smaller studies conclude that head injuries are a risk factor for dementia (125, 126). All 3 studies were well designed, but the small numbers of exposed cases limits any convincing conclusions. In addition, information bias is of concern in studying this question, since ascertaining the history of head injury requires recall of past events. Ascertaining the timing of the outcome (onset of dementia) is also clinically problematic and uncertain. In summary, findings regarding the role of MTBI as a risk factor for dementia should be considered inconclusive.

Is MTBI a risk factor for intracranial tumours?

Three accepted studies examined traumatic brain injury as a risk factor for development of intracranial tumours (127–129) (Table IV). The 2 cohort studies utilised national hospital databases from Denmark (128) and Sweden (129), and the case-control study (127) utilized data from a large American cancer registry and matched controls. In examining traumatic brain injury as a risk factor for tumours, diagnostic lead-time should be considered in order to ensure that the tumour was not present undetected at the time of the head injury. Both Nygren et al. (129) and Inskip et al. (128) utilized a 1-year buffer period to address this possibility; although Gurney et al. (127) did not. The larger confirmatory study (129) found no increased risk of brain tumour after head injury of any severity. However, in the exploratory cohort study (phase II) (128), a small increased risk was noted. Neither cohort study found any risk difference due to age; but the case-control study (127) reported an increased risk of brain tumour in children after head injury. This last study, though, was more susceptible to both diagnostic lead-time bias and recall bias, and the best evidence suggests little or no risk of brain tumour attributable to TBI.

Does whiplash injury result in cognitive deficits (MTBI)?

Because this was not our primary research question, no specific search was performed to attempt to capture all possible studies relating to this issue. However, studies of cognitive deficits after whiplash that were identified in our search were reviewed, as were studies cited in this literature and studies brought to our attention by members of the task force. We reviewed 22 studies on this topic and accepted 5 studies (Table V). These consisted of 1 phase II cohort (130), 1 cross-sectional (131) and 3 case series (132–134). Two of the case series report on 1 group of whiplash patients, and these studies suggest that subjective cognitive disturbances are frequent. However, objective cognitive testing failed to confirm the presence of these deficits (132, 134). The 2 stronger studies, a cohort and a cross-sectional study (130, 131) suggest that where cognitive deficits are found in patients with whiplash, these deficits are mild and likely associated with pain (130, 133), anxiety (133), pain medications and other psychosocial factors (130, 131), rather than brain damage (131). Given this evidence, it is unlikely that any long-term cognitive deficits in patients with whiplash are related to a mild brain injury.

DISCUSSION

We found only 2 acceptable phase III studies on prognosis for MTBI; 1 relating to risk of brain tumour and the other relating to the risk of epilepsy after MTBI. Of the cohort studies reporting children's prognosis for recovery after MTBI, approximately 85% were phase II, with the remainder being phase I. However,

Table IV. *Risk of epilepsy, dementia and brain tumour after mild traumatic brain injury (MTBI)*

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Annegers et al., 1998 (123)	Population-based. Olmstead county residents seeking medical care, head injury with LOC or skull fracture from 1935–84, MTBI classified as LOC or PTA <30 minutes (4541 MTBI cases)	53,222 person-years	Prognostic factors: time since injury. Outcome: risk of seizure disorder	Phase I cohort: Increased risk of seizure activity after MTBI. At 0–1 year SIR (95% CI) is 3.1 (1.0–7.2); at 1–4 years SIR = 2.1 (1.1–3.8); at 5–9 years, SIR = 0.9 (0.3–2.1). Overall, SIR = 1.5 (1.0–2.2)
Graves et al., 1990 (125).	Cases: Alzheimer's disease (n = 130). Controls: friend or non-blood relative of case, matched by age, sex (n = 130). Data obtained from surrogate (usually spouse)	Lifetime history of head injury	Prognostic factors: head injury with LOC or requiring medical care >1 year prior to onset of Alzheimer's, adjusted for age, family history. Outcome: risk of Alzheimer's disease	Case-control: TBI more common in Alzheimer's cases. Excluding head injuries within 5 years of onset: TBI with LOC (includes mild and severe TBI) OR = 2.5 (95% CI 1.0–6.4). For TBI without LOC, OR = 3.8 (95% CI 0.6–23.6)
Gurney et al., 1996 (127)	Cases: children <age 19 years with primary brain tumour (n = 540). Controls: children matched for age, gender, geographical regions (n = 801). No exclusion of tumour within 1 year of injury	Lifetime history of TBI	Prognostic factors: TBI, adjusting for number and severity of TBI, histology, birth injury and forceps delivery. Outcome: brain tumour	Case-control: Increased risk for developing brain tumour after MTBI. OR = 1.4 (95% CI 1.0–1.9)
Inskip et al., 1998 (128)	All patients in Denmark, discharge diagnosis related to head injury (fractured skull, concussion, cerebral laceration or contusion)	1,845,427 person years (average follow-up of 8.1 years)	Prognostic factors: MTBI adjusting for age, time since injury. Outcome: intracranial tumour	Phase I cohort: Excess risk in first year after MTBI likely due to detection of tumours already present. After first year, SIR (95% CI) of tumour after concussion was 1.2 (1.00–1.4). No age effect
Mehta et al., 1999 (124)	Community-based. 55 years and older, free of dementia at baseline (n = 6645)	Average follow-up 2 years	Prognostic factors: MTBI with LOC <15 minutes, adjusting for gender, number of TBI's and time since trauma. Outcome: dementia	Phase III cohort: No increased risk from TBI. RR (95% CI) for dementia was 1.0 (0.5–2.0) and for Alzheimer's RR = 0.8 (0.4–1.9). RR for dementia from >1 TBI was 1.4 (0.3–6.0)
Nygren et al., 2001 (129)	All patients in Sweden with discharge diagnosis related to skull trauma. Excluded those with brain tumour within 1 year of injury	3,225,317 person years (average follow-up 10.6 years)	Prognostic factors: TBI adjusted for gender and TBI severity. Outcome: primary brain tumour	Phase III cohort: No increased risk of brain tumour after a head injury of any severity (SIR was 1.0, 95% CI 0.9–1.2). No age effect
Schofield et al., 1997 (126)	Community-based. Adults aged >60 years, utilizing health services, not demented (n = 271)	0–5 years (median = 20.5 months)	Prognostic factor: MTBI adjusting for LOC, time since injury, age, alcohol problems Outcome: dementia	Phase II cohort: Increased risk of dementia for TBI defined by physician history RR = 3.2 (95% CI 1.2–8.6). For self-reported TBI, RR = 2.1 (95% CI 0.8–5.3). For TBI with LOC <= 5 minutes, RR = 1.7 (95% CI 0.4–7.5)

LOC = loss of consciousness; PTA = post-traumatic amnesia; SIR = standardized incidence ratio; 95% CI = 95% confidence intervals; TBI = traumatic brain injury; OR = odds ratio; RR = relative risk.

Table V. *Studies of cognitive deficits after whiplash injury*

Authors	Setting and subjects	Follow-up	Prognostic factors/outcomes	Design and findings
Karlsborg et al., 1997 (132); Smed, 1997 (134)	Patients reporting to emergency or neurology/neurosurgery departments; after whiplash injury without head trauma, seen within 14 days of injury ($n = 29$)	1 and 7 months	Prognostic factors: none Outcomes: cognitive tests, symptom checklist, psychological tests	Case series: Subjective complaints of cognitive disturbance were not supported by test results. No overall objective cognitive findings, and poor performance was associated with stressful life events
Olsnes, 1989 (131)	Outpatients. Cases: whiplash with persistent symptoms ($n = 34$). Controls: chronic pain patients, no history of trauma ($n = 21$)	None	Prognostic factors: whiplash trauma. Outcome: cognitive tests	Cross-sectional: At 6–18 months post-whiplash, cases had deficits on 4 of 48 cognitive tests compared with controls. One of these tests was still within normal limits. Authors conclude no evidence for brain damage from whiplash
Radanov et al., 1993 (130)	Referrals from physicians, with whiplash (no head blows). Cases: symptomatic at 6 months ($n = 31$). Controls: no symptoms at 6 months ($n = 67$)	6 months	Prognostic factors: persistent symptoms, adjusted for age, medications and education. Outcomes: cognitive tests.	Phase II cohort: Cognitive functioning at normal levels at 6 months. Symptomatic group showed slower recovery in complex attention, which may be related to medication effects
Radanov et al., 1999 (133)	Persistent post-whiplash complaints, including cognitive complaints, an average of 26 months post-injury; no head trauma or LOC, PTA, fractures or dislocations ($n = 21$, 17 were involved in litigation)	None	Prognostic factors: depression, anxiety, pain intensity. Outcomes: cognitive tests, neuroimaging	Case series: Average score on working memory and divided attention tasks were low. Both current (state) anxiety and pain intensity were associated with poorer performance on test of divided attention. No association between imaging findings and cognitive performance. Authors conclude that whiplash does not result in brain damage

LOC = loss of consciousness; PTA = post-traumatic amnesia.

of the cohort studies reporting prognosis after MTBI in adults, only half were phase II studies. This difference may account in part for the greater degree of variability in findings for the adult MTBI population, and this problem leads to less certainty in conclusions. Cross-sectional studies can also suggest hypotheses about outcome and prognostic factors, although this design makes it difficult to assess causal roles. Case series and descriptive studies can identify potential prognostic factors, but because the generalizability of these findings is poor and the potential for bias and confounding is high, such studies are very limited in their ability to provide meaningful information about prognosis.

The findings on prognosis for recovery after MTBI in children are quite consistent and positive. Drawing evidence from a variety of study designs, subject populations and comparing cases with a variety of control groups leads us to conclude that post-concussion symptoms and cognitive deficits are largely resolved within 2 or 3 months after MTBI in children. A number of studies point out the similarities between children sustaining a MTBI and those sustaining other kinds of injuries, suggesting that where deficits are observed, it is likely due to pre-morbid characteristics and/or the experience and aftermath of sustaining any injury.

The evidence for prognosis after MTBI in adults is less clear, partially because there has been less effective use of appropriate control groups and inadequate consideration of the possible confounding effect of other factors. The latter include pain, medications, the disabling effect of associated injuries, emotional distress and medicolegal or financial compensation factors. Follow-up is often too short to capture time to resolution of symptoms; or too long with no intervening follow-up periods, and there is no consideration of other factors that may have emerged in the interval that might explain the observed associations. Many measures of post-concussion symptoms ask subjects to identify symptoms that are either new or more intense since the injury, and thus may be seriously affected by failures of recall and/or reporting bias influenced by compensation issues. This is especially true when subjects are asked weeks, months or even years after the injury to recall pre-injury symptoms, injury-related events or acute post-injury symptoms.

The best evidence consistently suggests there are no MTBI-attributable, objectively measured, cognitive deficits beyond 1–3 months' post-injury in the majority of cases. Self-reported symptoms are common after MTBI; however there is little consistency in findings about how long such symptoms persist. On the other hand, symptoms usually resolve rapidly in athletes after a sports concussion, although it could be argued that they may under-report symptoms in order to resume play. With respect to other populations, the stronger studies of MTBI, which use appropriate control groups and consider the effects of other non-MTBI factors, generally show resolution of symptoms within weeks or a few months. There is also evidence that some of the observed long-standing post-concussion symptoms may be attributable to factors other than the MTBI. However, there is

a great need for well-designed, prospective, phase III confirmatory studies in this area.

Litigation and/or compensation have been consistently identified as prognostic of poor outcome in those cases that experience persistent symptoms and disability after MTBI, although again, no confirmatory study has been performed. Furthermore, a general lack of confirmatory studies similarly prevents firm conclusions about the role of other predictors of recovery after MTBI, although exploratory studies have suggested a number of possible factors, including mechanism of injury, pre-injury health, pain from associated injuries, and age. No study reported that severity of the MTBI was an independent predictor of persistent post-concussion symptoms. However, those sustaining more serious MTBI (e.g. GCS 13 or 14, focal brain lesions, depressed skull fractures) appear to have increased rates of disability, as assessed by the GOS or awarding of disability pensions. Most studies examining this issue, however, do not distinguish MTBI-related disabilities from those associated with injuries to other parts of the body. Thus, the independent role of severity of MTBI in long-term disability cannot be confirmed.

The best evidence suggests that MTBI increases the risk of seizures during the first 4 years post-injury, although the absolute risk is still low; but there is little or no increased risk of brain tumours following MTBI. No conclusions can yet be reached on the role of MTBI as a risk factor for dementia.

There is an ongoing debate as to whether whiplash injuries to the head and neck can commonly result in MTBI, and our task force reviewed the available evidence. The evidence shows that mild cognitive complaints do occur after whiplash, but are not specific to MTBI and are not likely due to a brain injury *per se*. These same cognitive complaints are also reported in patients with chronic pain (92), depression, anxiety, post-traumatic stress disorder, chronic fatigue syndrome, malingering and in patients involved in personal injury litigation (135).

CONCLUSION

The task force has found convincing evidence that, for children, prognosis for complete recovery after MTBI is good. Children suffering minor injuries frequently have transient symptoms regardless of whether the injury is MTBI or to some other part of the body. The evidence indicates that MTBI has little short- or long-term effect on cognitive functioning, school performance or behavioural development, and that post-concussion symptoms are largely resolved within 2–3 months of the injury. Where deficits in these areas are present, the determinants appear to be personal and social factors, rather than the MTBI itself. The mortality rate in children after MTBI is low, and studies report a minimum of 0% to a maximum of 0.25% death rate, where fatalities were characterized by an initial GCS score of 13 with subsequent deterioration. Although there are reports of disability as assessed by the GOS, most studies do not provide adequate information to clearly attribute the disability to the MTBI rather than to associated injuries.

Adults with MTBI frequently experience early cognitive deficits and post-concussion symptoms (most commonly headache) in the early weeks after the injury. However, there has been insufficient attention paid to the role of psychological distress or pain from associated injuries in the aetiology of these symptoms. Although the evidence indicates good recovery for most adults sustaining MTBI, where symptoms and disability are persistent, compensation and litigation factors are important, and exploratory studies suggest that prior health, age and life stressors are also determinants of poorer outcome. Future studies of prognosis in adults after MTBI should consider the confounding factors of pre-injury symptoms and personality characteristics, pre- and post-injury psychological distress, factors related to litigation and compensation and pain associated with injuries to other parts of the body.

ADDENDUM

Two recent studies (136, 137) concerning prognosis after MTBI in children came to the attention of our task force at our first presentation of findings at the 5th World Congress on Brain Injury (May, 2003). Time constraints did not permit a formal review of this research or inclusion in our best-evidence synthesis. However, the studies are phase II cohorts, with long-term follow-up of the same birth cohort of children with MTBI, and the findings are notably discrepant from other strong evidence included in this report. These findings, which need to be reproduced in other samples, definitely raise the possibility of an association between MTBI and later onset of hyperactivity/inattention and conduct disorder, especially in children under the age of 5 years who were hospitalized for MTBI.

ACKNOWLEDGEMENTS

This work was supported by a grant from Saskatchewan Government Insurance, Canada; the Insurance Corporation of British Columbia, Canada; La Société de l'assurance automobile du Québec, Canada; AFA Insurance Sweden; Folksam Insurance, Sweden; the Volvo Car Company, Sweden; and Trygg-Hansa, Sweden. Drs Cassidy and Carroll are supported by Health Scholar Awards from the Alberta Heritage Foundation for Medical Research.

REFERENCES

1. Cassidy JD, Carroll LJ, Peloso PM, Borg J, von Holst H, Holm L, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; (suppl 43): 28–60.
2. Altman DG. Methodological challenges in the evaluation of prognostic factors in breast cancer. Breast Cancer Res Treat 1998; 52: 289–303.
3. Côté P, Cassidy JD, Carroll LJ, Frank JW, Bombardier C. A systematic review of the prognosis of acute whiplash and a new conceptual framework to synthesize the literature. Spine 2001; 26: E445–E458.
4. Carroll LJ, Cassidy JD, Peloso PM, Garritty C, Giles-Smith L. Systematic search and review procedures: results of the WHO

Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; (suppl 43): 11–14.
5. Cassidy JD, Carroll LJ, Côté P, Holm L, Nygren Å. Mild traumatic brain injury after traffic collisions: a population-based cohort study. J Rehabil Med 2004; (suppl 43): 15–21.
6. Peloso PM, von Holst H, Borg J. Mild traumatic brain injuries presenting to hospitals in Sweden during the years 1987 to 2000. J Rehabil Med 2004; (suppl 43): 22–27.
7. Slavin RE. Best evidence synthesis: an alternative to meta-analytic and traditional reviews. Educational Researcher 1986; 15: 5–11.
8. Slavin RE. Best evidence synthesis: an intelligent alternative to meta-analysis. J Clin Epidemiol 1995; 48: 9–18.
9. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld J. Recovery of intellectual ability following traumatic brain injury in childhood: Impact of injury severity and age at injury. Pediatr Neurosurg 2000; 32: 282–290.
10. Anderson VA, Catroppa C, Rosenfeld J, Haritou F, Morse SA. Recovery of memory function following traumatic brain injury in pre-school children. Brain Inj 2000; 14: 679–692.
11. Bijur PE, Haslum M, Golding J. Cognitive and behavioral sequelae of mild head injury in children. Pediatrics 1990; 86: 337–344.
12. Bijur PE, Haslum M, Golding J. Cognitive outcomes of multiple mild head injuries in children. J Dev Behav Pediatr 1996; 17: 143–148.
13. Farmer MY, Singer HS, Mellits ED, Hall D, Charney E. Neurobehavioral sequelae of minor head injuries in children. Pediatr Neurosci 1987; 13: 304–308.
14. Fay GC, Jaffe KM, Polissar NL, Liao S, Martin KM, Shurtleff HA, et al. Mild pediatric traumatic brain injury: a cohort study. Arch Phys Med Rehabil 1993; 74: 895–901.
15. Fay GC, Jaffe KM, Polissar NL, Liao S, Rivara JB, Martin KM. Outcome of pediatric traumatic brain injury at three years: a cohort study. Arch Phys Med Rehabil 1994; 75: 733–741.
16. Fletcher JM, Ewing CL, Miner ME, Levin HS, Eisenberg HM. Behavioral changes after closed head injury in children. J Consult Clin Psychol 1990; 58: 93–98.
17. Greenspan AI, MacKenzie EJ. Functional outcome after pediatric head injury. Pediatrics 1994; 94: 425–432.
18. Jaffe KM, Fay GC, Polissar NL, Martin KM, Shurtleff H, Rivara JB, et al. Severity of pediatric traumatic brain injury and early neurobehavioral outcome: a cohort study. Arch Phys Med Rehabil 1992; 73: 540–547.
19. Jaffe KM, Fay GC, Polissar NL, Martin KM, Shurtleff HA, Rivara JM, et al. Severity of pediatric traumatic brain injury and neurobehavioral recovery at one year–a cohort study. Arch Phys Med Rehabil 1993; 74: 587–595.
20. Jaffe KM, Polissar NL, Fay GC, Liao S. Recovery trends over three years following pediatric traumatic brain injury. Arch Phys Med Rehabil 1995; 76: 17–26.
21. Kaufmann PM, Fletcher JM, Levin HS, Miner ME, Ewing CL. Attentional disturbance after pediatric closed head injury. J Child Neurol 1993; 8: 348–353.
22. Kinsella G, Ong B, Murtagh D, Prior M, Sawyer M. The role of the family for behavioral outcome in children and adolescents following traumatic brain injury. J Consult Clin Psychol 1999; 67: 116–123.
23. Kraus JF, Fife D, Conroy C. Pediatric brain injuries: the nature, clinical course, and early outcomes in a defined United States' population. Pediatrics 1987; 79: 501–507.
24. Lazar L, Erez I, Gutermacher M, Katz S. Brain concussion produces transient hypokalemia in children. J Pediatr Surg 1997; 32: 88–90.
25. Levi L, Guilburd JN, Linn S, Feinsod M. The association between skull fracture, intracranial pathology and outcome in pediatric head injury. Br J Neurosurg 1991; 5: 617–625.
26. Light R, Asarnow R, Satz P, Zaucha K, McCleary C, Lewis R. Mild closed-head injury in children and adolescents: behavior problems and academic outcomes. J Consult Clin Psychol 1998; 66: 1023–1029.
27. Luerssen TG, Klauber MR, Marshall LF. Outcome from head injury related to patient's age. A longitudinal prospective study of adult and pediatric head injury. J Neurosurg 1988; 68: 409–416.
28. Ong L, Selladurai BM, Dhillon MK, Atan M, Lye MS. The prognostic value of the Glasgow Coma Scale, hypoxia and computerised tomography in outcome prediction of pediatric head injury. Pediatr Neurosurg 1996; 24: 285–291.
29. Polissar NL, Fay GC, Jaffe KM, Liao S, Martin KM, Shurtleff HA, et al. Mild pediatric traumatic brain injury: adjusting significance levels for multiple comparisons. Brain Inj 1994; 8: 249–263.
30. Ponsford J, Willmott C, Rothwell A, Cameron P, Ayton G, Nelms R, et al. Cognitive and behavioral outcome following mild traumatic head injury in children. J Head Trauma Rehabil 1999; 14: 360–372.
31. Rivara JB, Fay GC, Jaffe KM, Polissar NL, Shurtleff HA, Martin KM. Predictors of family functioning one year following traumatic brain injury in children. Arch Phys Med Rehabil 1992; 73: 899–910.
32. Rivara JB, Jaffe KM, Fay GC, Polissar NL, Martin KM, Shurtleff HA, et al. Family functioning and injury severity as predictors of child functioning one year following traumatic brain injury. Arch Phys Med Rehabil 1993; 74: 1047–1055.
33. Rivara JM, Jaffe KM, Polissar NL, Fay GC, Liao S, Martin KM. Predictors of family functioning and change 3 years after traumatic brain injury in children. Arch Phys Med Rehabil 1996; 77: 754–764.
34. Wrightson P, McGinn V, Gronwall D. Mild head injury in preschool children: evidence that it can be associated with a persisting cognitive defect. J Neurol Neurosurg Psychiatry 1995; 59: 375–380.
35. Yorkston KM, Jaffe KM, Polissar NL, Liao S, Fay GC. Written language production and neuropsychological function in children with traumatic brain injury. Arch Phys Med Rehabil 1997; 78: 1096–1102.
36. Yorkston KM, Jaffe KM, Liao S, Polissar NL. Recovery of written language production in children with traumatic brain injury: outcomes at one year. Aphasiology 1999; 13: 691–700.
37. Basson MD, Guinn JE, McElligott J, Vitale R, Brown W, Fielding LP. Behavioral disturbances in children after trauma. J Trauma 1991; 31: 1363–1368.
38. Hahn YS, Fuchs S, Flannery AM, Barthel MJ, McLone DG. Factors influencing posttraumatic seizures in children. Neurosurgery 1988; 22: 864–867.
39. Hahn YS, McLone DG. Risk factors in the outcome of children with minor head injury. Pediatr Neurosurg 1993; 19: 135–142.
40. Jennett B, Bond M. Assessment of outcome after severe brain damage: a practical scale. Lancet 1975; 1: 480–484.
41. Wilson JTL, Pettigrew LEL, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the Extended Glasgow Outcome Scale: guidelines for their use. J Neurotrauma 1998; 15: 573–597.
42. Bazarian JJ, Wong T, Harris M, Leahey N, Mookerjee S, Dombovy M. Epidemiology and predictors of post-concussive syndrome after minor head injury in an emergency population. Brain Inj 1999; 13: 173–189.
43. Ommaya AK, Salazar AM, Dannenberg AL, Chervinsky AB, Schwab K. Outcome after traumatic brain injury in the U.S. military medical system. J Trauma 1996; 41: 972–975.
44. Teasdale TW, Engberg A. Duration of cognitive dysfunction after concussion, and cognitive dysfunction as a risk factor: a population study of young men. BMJ 1997; 315: 569–572.
45. Bryant RA, Harvey AG. Relationship between acute stress disorder and posttraumatic stress disorder following mild traumatic brain injury. Am J Psychiatry 1998; 155: 625–629.
46. Dikmen SS, Machamer JE, Donovan DM, Winn HR, Temkin NR. Alcohol use before and after traumatic head injury. Ann Emerg Med 1995; 26: 167–176.
47. Dikmen SS, Machamer JE, Winn HR, Temkin NR. Neuropsychological outcome at 1-year post head injury. Neuropsychology 1995; 9: 80–90.
48. Garraway M, Macleod D. Epidemiology of rugby football injuries. Lancet 1995; 345: 1485–1487.
49. Greiffenstein FM, Baker JW. Comparison of premorbid and postinjury MMPI-2 profiles in late postconcussion claimants. Clin Neuropsychol 2001; 15: 162–170.
50. Harvey AG, Bryant RA. Acute stress disorder after mild traumatic brain injury. J Nerv Ment Dis 1998; 186: 333–337.

51. Hsiang JN, Yeung T, Yu AL, Poon WS. High-risk mild head injury. J Neurosurg 1997; 87: 234–238.
52. Kraus JF, Fife D. Incidence, external causes, and outcomes of work-related brain injuries in males. J Occup Med 1985; 27: 757–760.
53. Macciocchi SN, Barth JT, Alves W, Rimel RW, Jane JA. Neuropsychological functioning and recovery after mild head injury in collegiate athletes. Neurosurgery 1996; 39: 510–514.
54. Maddocks D, Saling M. Neuropsychological deficits following concussion. Brain Inj 1996; 10: 99–103.
55. McCrory PR, Ariens T, Berkovic SF. The nature and duration of acute concussive symptoms in Australian football. Clin J Sport Med 2000; 10: 235–238.
56. McMillan TM, Glucksman EE. The neuropsychology of moderate head injury. J Neurol Neurosurg Psychiatry 1987; 50: 393–397.
57. Teasdale TW, Engberg AW. Disability pensions in relation to traumatic brain injury: a population study. Brain Inj 2000; 14: 363–372.
58. Williams DH, Levin HS, Eisenberg HM. Mild head injury classification. Neurosurgery 1990; 27: 422–428.
59. Lovell MR, Iverson GL, Collins MW, McKeag D, Maroon JC. Does loss of consciousness predict neuropsychological decrements after concussion? Clin J Sport Med 1999; 9: 193–198.
60. Benson BW, Rose MS, Meeuwisse WH. The impact of face shield use on concussions in ice hockey: a multivariate analysis. Br J Sports Med 2002; 36: 27–32.
61. Bryant RA, Harvey AG. The influence of traumatic brain injury on acute stress disorder and post-traumatic stress disorder following motor vehicle accidents. Brain Inj 1999; 13: 15–22.
62. Friedland JF, Dawson DR. Function after motor vehicle accidents: a prospective study of mild head injury and posttraumatic stress. J Nerv Ment Dis 2001; 189: 426–434.
63. Gennarelli TA, Champion HR, Copes WS, Sacco WJ. Comparison of mortality, morbidity, and severity of 59,713 head injured patients with 114,447 patients with extracranial injuries. J Trauma 1994; 37: 962–968.
64. Hanks RA, Temkin N, Machamer J, Dikmen SS. Emotional and behavioral adjustment after traumatic brain injury. Arch Phys Med Rehabil 1999; 80: 991–997.
65. Kraus JF, Morgenstern H, Fife D, Conroy C, Nourjah P. Blood alcohol tests, prevalence of involvement, and outcomes following brain injury. Am J Public Health 1989; 79: 294–299.
66. Masson F, Maurette P, Salmi LR, Dartigues JF, Vecsey J, Destaillats JM, et al. Prevalence of impairments 5 years after a head injury, and their relationship with disabilities and outcome. Brain Inj 1996; 10: 487–497.
67. Paniak C, Reynolds S, Toller-Lobe G, Melnyk A, Nagy J, Schmidt D. A longitudinal study of the relationship between financial compensation and symptoms after treated mild traumatic brain injury. J Clin Exp Neuropsychol 2002; 24: 187–193.
68. Paniak C, Reynolds S, Phillips K, Toller-Lobe G, Melnyk A, Nagy J. Patient complaints within 1 month of mild traumatic brain injury: a controlled study. Arch Clin Neuropsychol 2002; 17: 319–334.
69. Paniak C, Toller-Lobe G, Melnyk A, Nagy J. Prediction of vocational status three to four months after treated mild traumatic brain injury. J Musculoske Pain 2000; 8: 193–200.
70. Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly AM, Nelms R, et al. Factors influencing outcome following mild traumatic brain injury in adults. J Int Neuropsychol Soc 2000; 6: 568–579.
71. Riemann BL, Guskiewicz KM. Effects of mild head injury on postural stability as measured through clinical balance testing. J Athl Training 2002; 35: 19–25.
72. Selladurai BM, Vickneswaran M, Duraisamy S, Atan M. Coagulopathy in acute head injury-a study of its role as a prognostic indicator. Br J Neurosurg 1997; 11: 398–404.
73. Thornhill S, Teasdale GM, Murray GD, McEwen J, Roy CW, Penny KI. Disability in young people and adults one year after head injury: prospective cohort study. BMJ 2000; 320: 1631–1635.
74. Lowdon IM, Briggs M, Cockin J. Post-concussional symptoms following minor head injury. Injury 1989; 20: 193–194.
75. Binder LM, Rohling ML. Money matters: a meta-analytic review of the effects of financial incentives on recovery after closed-head injury. Am J Psychiatry 1996; 153: 7–10.
76. Bohnen N, Van Zutphen W, Twijnstra A, Wijnen G, Bongers J, Jolles J. Late outcome of mild head injury: results from a controlled postal survey. Brain Inj 1994; 8: 701–708.
77. Matser JT, Kessels AG, Lezak MD, Troost J. A dose-response relation of headers and concussions with cognitive impairment in professional soccer players. J Clin Exp Neuropsychol 2001; 23: 770–774.
78. Ferguson RJ, Mittenberg W, Barone DF, Schneider B. Postconcussion syndrome following sports-related head injury: expectation as etiology. Neuropsychology 1999; 13: 582–589.
79. Gentilini M, Nichelli P, Schoenhuber R, Bortolotti P, Tonelli L, Falasca A, et al. Neuropsychological evaluation of mild head injury. J Neurol Neurosurg Psychiatry 1985; 48: 137–140.
80. Iverson GL, Lovell MR, Smith SS. Does brief loss of consciousness affect cognitive functioning after mild head injury? Arch Clin Neuropsychol 2000; 15: 643–648.
81. Matser EJ, Kessels AG, Lezak MD, Jordan BD, Troost J. Neuropsychological impairment in amateur soccer players. JAMA 1999; 282: 971–973.
82. Paniak C, Phillips K, Toller-Lobe G, Durand A, Nagy J. Sensitivity of three recent questionnaires to mild traumatic brain injury-related effects. J Head Trauma Rehabil 1999; 14: 211–219.
83. Richardson JT, Snape W. The effects of closed head injury upon human memory: an experimental analysis. Cognit Neuropsychol 1984; 1: 217–231.
84. Richardson JT, Barry C. The effects on minor closed head injury upon human memory: further evidence on the role of mental imagery. Cognit Neuropsychol 1985; 2: 149–168.
85. Bryant RA, Harvey AG. Postconcussive symptoms and posttraumatic stress disorder after mild traumatic brain injury. J Nerv Ment Dis 1999; 187: 302–305.
86. Amacher AL, Bybee DE. Toleration of head injury by the elderly. Neurosurgery 1987; 20: 954–958.
87. Crawford S, Wenden FJ, Wade DT. The Rivermead head injury follow-up questionnaire: a study of a new rating scale and other measures to evaluate outcome after head injury. J Neurol Neurosurg Psychiatry 1996; 60: 510–514.
88. Boyd CR, Usher CH, Wirth FP, Downing EF, Baker RP, Cannon CL, et al. Head injury at the southeastern Georgia Regional Trauma Center: a three-year review. J Med Assoc Ga 1989; 78: 341–344.
89. Cline DM, Whitley TW. Observation of head trauma patients at home: a prospective study of compliance in the rural south. Ann Emerg Med 1988; 17: 127–131.
90. Dunn LT, Patterson M, Boot DA. Head injury in the severely injured: long-term follow-up in 157 patients. Br J Neurosurg 2000; 14: 219–224.
91. Fee CR, Rutherford WH. A study of the effect of legal settlement on post-concussion symptoms. Arch Emerg Med 1988; 5: 12–17.
92. Iverson GL, McCracken LM. "Postconcussive" symptoms in persons with chronic pain. Brain Inj 1997; 11: 783–790.
93. Lee ST, Lui TN. Early seizures after mild closed head injury. J Neurosurg 1992; 76: 435–439.
94. Lidvall HF, Linderoth B, Norlin B. Causes of the post-concussional syndrome: IX. Psychological tests. Acta Neurol Scand 1974; 50; (suppl 56): 64–71.
95. Lidvall H, Linderoth B, Norlin B. Causes of the post-concussional syndrome: III. Principal features of the investigation. Acta Neurol Scand 1974; 50 (suppl 56): 19–22.
96. Maddocks DL, Saling M, Dicker GD. A note on normative data for a test sensitive to concussion in Australian Rules footballers. Aust Psychol 1995; 30: 125–127.
97. McGhee CN, Gullan RW, Miller JD. Motorcycling and head injury: admissions to a regional head injury unit. Br J Neurosurg 1987; 1: 271–275.
98. Miller JD, Murray LS, Teasdale GM. Development of a traumatic intracranial hematoma after a "minor" head injury. Neurosurgery 1990; 27: 669–673.
99. Miller LJ, Donders J. Subjective symptomatology after traumatic head injury. Brain Inj 2001; 15: 297–304.
100. Pentland B, Jones PA, Roy CW, Miller JD. Head injury in the elderly. Age Ageing 1986; 15: 193–202.
101. Ritchie PD, Cameron PA, Ugoni AM, Kaye AH. A study of the

functional outcome and mortality in elderly patients with head injuries. J Clin Neurosci 2000; 7: 301–304.
102. Rutherford W, Merrett JD, McDonald JR. Symptoms at one year following concussion from minor head injuries. Injury 1979; 10: 225–230.
103. Rutherford W, Merrett JD, McDonald JR. Sequelae of concussion caused by minor head injuries. Lancet 2002; 1: 1–4.
104. Carroll LJ, Cassidy JD, Holm L, Kraus J, Coronado V. Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004; (suppl 43): 113–125.
105. King NS, Crawford S, Wenden FJ, Moss NE, Wade DT. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. J Neurol 1995; 242: 587–592.
106. Kay T, Cavallo MM, Ezrachi O, Vavagiakis P. The Head Injury Family Interview: a clinical and research tool. J Head Trauma Rehabil 1995; 10: 12–31.
107. Ware JE, Jr, Snow KK, Kosinski M, Gandek B. SF-36 health survey: manual and interpretation guide. Boston (MA): The Health Institute, New England Medical Center; 1993.
108. Willer B, Linn R, Allen K. Community integration and barriers to integration for individuals with brain injury. In: Finlayson MAJ, Garner S, eds. Brain Injury Rehabilitation: Clinical Considerations. Baltimore (MD): Williams & Wilkins; 1993, p. 355–375.
109. American Psychological Association. Diagnostic and statistical manual of mental disorders: DSM-IV. 4th edn. Washington, D.C.: American Psychological Association; 1994.
110. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. 10th edn. Geneva: World Health Organization; 1992.
111. Binder LM. Assessment of malingering after mild head trauma with the Portland Digit Recognition Test [published erratum appears in J Clin Exp Neuropsychol 1993; 15: 852]. J Clin Exp Neuropsychol 1993; 15: 170–182.
112. Greiffenstein MF, Baker WJ, Gola T. Comparison of multiple scoring methods for Rey's malingered amnesia measures. Toxicol Lett 1996; 11: 283–293.
113. Binder LM, Villanueva MR, Howieson D, Moore RT. The Rey AVLT recognition memory task measures motivational impairment after mild head trauma. Arch Clin Neuropsychol 1993; 8: 137–147.
114. Green P, Iverson GL, Allen L. Detecting malingering in head injury litigation with the Word Memory Test. Brain Inj 1999; 13: 813–819.
115. Greiffenstein MF, Baker WJ, Gola T. Validation of malingered amnesia measures with a large clinical sample. Psychol Assess 1994; 6: 218–224.
116. Greiffenstein MF, Baker WJ, Gola T. Motor dysfunction profiles in traumatic brain injury and postconcussion syndrome. J Int Neuropsychol Soc 1996; 2: 477–485.
117. Keller M, Hiltbrunner B, Dill C, Kesselring J. Reversible neuropsychological deficits after mild traumatic brain injury. J Neurol Neurosurg Psychiatry 2000; 68: 761–764.
118. Millis SR, Putnam SH, Adams KM, Ricker JH. The California Verbal Learning Test in the detection of incomplete effort in neuropsychological evaluation. Psychol Assess 1995; 7: 463–471.
119. Millis SR, Ross SR, Ricker JH. Detection of incomplete effort on the Wechsler Adult Intelligence Scale-Revised: a cross-validation. J Clin Exp Neuropsychol 1998; 20: 167–173.
120. Suhr J, Tranel D, Wefel J, Barrash J. Memory performance after head injury: contributions of malingering, litigation status, psychological factors, and medication use. J Clin Exp Neuropsychol 1997; 19: 500–514.
121. Suhr JA, Boyer D. Use of the Wisconsin Card Sorting Test in the detection of malingering in student simulator and patient samples. J Clin Exp Neuropsychol 1999; 21: 701–708.
122. Annegers JF, Grabow JD, Groover RV, Laws ER, Jr, Elveback LR, Kurland LT. Seizures after head trauma: a population study. Neurology 1980; 30: 683–689.
123. Annegers JF, Hauser WA, Coan SP, Rocca WA. A population-based study of seizures after traumatic brain injuries. N Engl J Med 1998; 338: 20–24.
124. Mehta KM, Ott A, Kalmijn S, Slooter AJ, van Duijn CM, Hofman A, et al. Head trauma and risk of dementia and Alzheimer's disease: the Rotterdam Study. Neurology 1999; 53: 1959–1962.
125. Graves AB, White E, Koepsell TD, Reifler BV, van Belle G, Larson EB, et al. The association between head trauma and Alzheimer's disease. Am J Epidemiol 1990; 131: 491–501.
126. Schofield PW, Tang M, Marder K, Bell K, Dooneief G, Chun M, et al. Alzheimer's disease after remote head injury: an incidence study. J Neurol Neurosurg Psychiatry 1997; 62: 119–124.
127. Gurney JG, Preston MS, McDaniel AM, Mueller BA, Holly EA. Head injury as a risk factor for brain tumors in children: results from a multicenter case-control study. Epidemiology 1996; 7: 485–489.
128. Inskip PD, Mellemkjaer L, Gridley G, Olsen JH. Incidence of intracranial tumors following hospitalization for head injuries. Cancer Causes Control 1998; 9: 109–116.
129. Nygren C, Adami J, Ye W, Bellocco R, af Geijerstam J-L, Borg J, et al. Primary brain tumors following traumatic brain injury–a population-based cohort study in Sweden. Cancer Causes Control 2001; 12: 733–737.
130. Radanov BP, Di Stefano G, Schnidrig A, Sturzenegger M, Augustiny KF. Cognitive functioning after common whiplash: a controlled follow-up study. Arch Neurol 1993; 50: 87–91.
131. Olsnes BT. Neurobehavioral findings in whiplash patients with long-lasting symptoms. Acta Neurol Scand 1989; 80: 584–588.
132. Karlsborg M, Smed A, Jespersen H, Stephensen S, Cortsen M, Jennum P, et al. A prospective study of 39 patients with whiplash injury. Acta Neurol Scand 1997; 95: 65–72.
133. Radanov BP, Bicik I, Dvorak J, Antinnes J, von Schulthess GK, Buck A. Relation between neuropsychological and neuroimaging findings in patients with late whiplash syndrome. J Neurol Neurosurg Psychiatry 1999; 66: 485–489.
134. Smed A. Cognitive function and distress after common whiplash injury. Acta Neurol Scand 1997; 95: 73–80.
135. Alexander M. The evidence for brain injury in whiplash injuries. Pain Res Manage 2003; 8: 19–23.
136. McKinlay A, Dalrymple-Alford JC, Horwood LJ, Fergusson DM. Long-term psychosocial outcomes after mild head injury in early childhood. J Neurol Neurosurg Psychiatry 2002; 73: 281–288.
137. McKinlay A, Dalrymple-Alford JC, Horwood LJ, Fergusson DM. Pre-injury and other non-specific factors do not explain adverse psychosocial development associated with childhood mild head injury [abstract]. Brain Inj 2003; 17 (suppl 1): 39.