Prognostic Factors for Persistent Symptoms in Adults With Mild Traumatic Brain Injury: Protocol for an Overview of Systematic Reviews

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Protocol

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Abstract

Background: Mild traumatic brain injury (mTBI) is an increasing public health problem, and persistent symptoms following mTBI have several functional consequences. Understanding the prognosis of a condition is an important component of clinical decision-making and can help to guide prevention of long-term disabilities and to intervene with mTBI patients. Prognosis of chronic symptoms in mTBI has stimulated several empirical primary research papers and many systematic reviews. We aim to integrate these heterogenous factors into a model in order to have a better understanding of such prognostic factors on the development of chronic symptoms.

Methods: We will conduct an overview of systematic reviews following steps described in the Cochrane Handbook. We will search for systematic reviews in databases using a search strategy to include articles that review evidence about prognosis of persistent symptoms after an mTBI in the adult population. Two reviewers will independently screen all references and then select eligible reviews based on eligibility criteria. Any disagreements will be discussed by the two reviewers and if consensus is not reached, we will consult a third reviewer. A data extraction grid will be used to extract relevant information. The risk of bias included will be rated using ROBIS tool. Data will be synthesized into a comprehensive conceptual map in order to have a better understanding of the predictor factors that could impact the recovery after mTBI.

Discussion: Results will help multiple stakeholders, such as clinicians and rehabilitation program managers, to understand the prognosis of long-term consequences following an mTBI. It could guide stakeholders to recognize predisposing, precipitating, and perpetuating factors of their patients and to invest their time and resources on patients needing the most.

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Background

Cases of mild traumatic brain injury (mTBI) have increased in the past few years (1, 2), and the long-lasting effects have received increasing attention (3). Most of the symptoms disappear in a few days or weeks (4), but 5–20% of sufferers encounter persistent physical, cognitive, and behavioural disabilities (5). Most prevalent chronic symptoms are headaches, difficulty concentrating, fatigue, and dizziness (6). These chronic symptoms can have important impacts on day-to-day activities and can lead to functional consequences such as delays in return to work (7, 8). To prevent the persistent symptoms of mTBI, it is important to identify and understand factors that can interfere with a normal recovery, such as depression, chronic pain, or situational stress (9). To recognize symptoms and to diagnose mTBI is a good start but identifying what contributes to persistent symptoms in the target population would help healthcare providers to target the right patients and to intervene on these factors before symptoms become chronic.

Understanding a condition's prognosis is an important component of clinical decision-making (10). Many factors can be related to a positive or poor prognosis in a given condition. Identifying prognostic factors that can contribute to poor prognosis in mTBI is important in order to better understand this condition and to target patients with the greatest needs (10). Patients with a poor prognosis should arguably be considered for more in depth evaluation and targeted intervention in the early stages of the condition in order to prevent a transition to chronicity. In fact, persistent disability from mTBI could be reduced by identifying and addressing earlier risk factors, such as comorbidities (e.g. depression, anxiety, etc.) (11, 12). Long-lasting symptoms after mTBI are both complex and nonspecific, which highlights the need to identify subgroups of the mTBI population that might benefit from specific and early interventions (12).

Over the past years, several studies and reviews have focused on possible factors contributing to persistent disabling problems after suffering an mTBI. The World Health Organization (WHO) Collaborating Centre Task Force has produced an extensive number of systematic reviews related to prognosis for mTBI (2–4, 12–19). These reviews mainly synthesized studies employing longitudinal design to identify time to recovery and prognostic factors affecting recovery or symptom persistence (15). Various and numerous factors were identified as predictors of prolonged symptoms or associated with slower recovery, such as financial compensation, being married, being off work due to the injury, post injury symptoms of nausea or memory problems and other injuries (percentage of the body in pain after the collision), pre-existing physical limitations, prior brain illness or neurological problems, prior head injuries, psychiatric problems, life stressors, being a student, sustaining mTBI in a motor vehicle collision, and age over 40 years (15). However, to our knowledge, no global systematic mapping has been synthesized based on reviews related to prognostic factors of persistent symptoms after mTBI. We found that authors summarized findings of the International Collaboration on Mild Traumatic Brain Injury Prognosis (20), but no systematic research strategy has been used and results have not yet been integrated into a comprehensive model, such as the one presented in Hou et al. (21). There are a growing number of systematic reviews specifically investigating prognostic information, prognostic models, prognostic variables, or risk prediction models (22). We aim to combine all prognostic factors into a conceptual model in order to have a usable and comprehensive document to clearly address the predictors of chronic symptoms. Considering the large body of evidence published, it would be relevant to conduct a synthesis of systematic reviews related to this subject. An overview of systematic reviews is a rigorous approach to mapping evidence of a large body of literature in a given area (22, 23). Nomenclature and methods used for this type of review vary in the literature: 'umbrella reviews', 'meta-reviews', 'overviews of systematic reviews', 'reviews of reviews', and 'a systematic review of systematic reviews', among others (24). The approach requires similar search strategies and quality scoring as a systematic review of primary literature, but relies on the appraisal and data extraction of previous reviewers rather than a return to primary sources (25, 26).

Objectives

Our objective is to synthesize evidence from systematic reviews about factors that affect the risk of chronic or persistent symptoms in mTBI adults. We aim more specifically to gather information about 1) predisposing factors; 2) precipitating factors; and 3) the contribution of cognitive, emotional, behavioural, and social perpetuating factors in the development of persistent symptoms.

Methods

To achieve this objective, we will conduct an overview of systematic reviews according to the principles of the Cochrane Handbook's chapter on methods for overviews of reviews (25) and other recent methodological papers (27–29). Overview of reviews (OvR) is designed to compile, synthesize, and integrate evidence from multiple systematic reviews into one accessible and usable document (25, 27). Despite their increasing popularity in healthcare research over the past years, there are currently no systematically developed reporting guidelines for OvR (24, 30). However, this protocol has been prepared in consultation with the PRISMA-P statement (31) (checklist provided in the supplemental documents to this protocol, in the additional file). This review has been registered in the PROSPERO database (CRD42020176676). Any amendments to the protocol will be described in the final review article.

Literature searches

A professional librarian and members of the research team will help to develop the search strategy based on the objective of the review. We used the PICO model to develop our search strategy: 1) MTBI/concussion (patient); 2) Chronic/persistent symptoms (intervention); 3) Prognosis (outcome); and 4) Systematic review (types of study). The "comparison" concept is not relevant for our review, and we chose to add a "types of study" concept considering that we will focus our search on systematic reviews only. We will search in five relevant databases (Cochrane (Wiley), Medline (Ovid), CINAHL (EBSCO), Embase (Elsevier), PsycINFO (Ovid)) for systematic reviews published in peer-reviewed journals without date restrictions. An example of a search strategy in Medline (Ovid) is displayed in Table 1.

Table 1
Example of search strategy in Medline (Ovid) database

1) Concept : MTBI concussion		
#1	[ti.]	(concuss* OR commotio* cerebr* OR cerebral* commotio* OR mtbi) or ((mild OR minor OR minimal) adj3 (traumatic brain OR tbi))
#2	[ab.]	(concuss* OR commotio* cerebr* OR cerebral* commotio* OR mtbi) OR ((mild OR minor OR minimal) adj3 (traumatic brain OR tbi))
#3	[Mesh]	Brain injuries, traumatic/
#4	[Mesh]	Brain concussion/
#5	#1 OR #2 OR #3 OR #4	
2) Concept : **Chronic/persistent symptoms**		
#6	[ti.]	(prolong* OR persist* OR unresolved OR delay* OR chronic* OR post-concuss* OR postconcuss*)
#7	[ab.]	(prolong* OR persist* OR unresolved OR delay* OR chronic* OR post-concuss* OR postconcuss*)
#8	[Mesh]	Post-Concussion Syndrome/
#9	#6 OR #7 OR #8	
3) Concept: **Prognosis**		
#10	[ti.]	(prognos* OR predict* OR course* OR outcome*)
#11	[ab.]	(prognos* OR predict* OR course* OR outcome*)
#12	[Mesh]	Prognosis/
#13	#10 OR #11 OR #12	
#14	#5 AND #9 AND #13	
4) Concept: **Systematic reviews**		
#15	[pt.]	Systematic review
#16	**#14 AND #15**	

Eligibility criteria

We will only include studies that have employed a systematic review design, peer-reviewed systematic reviews, or meta-analyses. We will consider publications to be systematic reviews if they were clearly described in the report as being based on a systematic search, by precisely presenting the search strategy and the selection process of the articles (such as a PRISMA flow diagram). French or English publications will be included. We will consider reviews targeting only adult populations with mTBI or concussion. In order to have a common definition of the condition, we will refer to the WHO Collaborating Centre Task

Force on Mild Traumatic Brain Injury definition (32). We will include manuscripts that reviewed the course of at least one persistent symptom in mTBI patients. Narrative, non-systematic reviews, editorials/ commentaries, or grey literature, such as thesis work, will not be eligible for this OvR. We will also exclude reviews about moderate, severe, or non-traumatic brain injuries, and reviews targeting a child population.

Data management

All references will be imported from the databases in a reference management software (Endnote). Duplicates will be removed using the software command “Find duplicates” based on the title of the references. Then, once duplicates have been removed, the screening and selection process will be performed by using Covidence online software (33).

Screening and selection process

Two reviewers will independently screen all references identified from the literature search. All references judged potentially eligible after screening for title and abstract will be reviewed in a full text. Any disagreement will be discussed by the two reviewers, and if consensus is not reached, we will consult a third member of the team.

Data extraction

Relevant information from all selected reviews will be grouped in an extraction grid. We will create the grid and extract data from the reviews, such as study details (authors, year of publication, dates of search, design, number of studies included, types of analysis, purpose of the reviews, etc.), population studied, prognostic factors, outcomes measured (mainly post-concussion symptoms), post-injury timeframe, and other relevant results found in the reviews. Extraction will be limited to information presented in the included systematic reviews and not in the primary research studies (26). Two independent reviewers will extract data and then will compare their respective grid and reach a consensus.

Risk of bias assessment

Risk of bias of the included reviews will be rated using the Risk of Bias in Systematic Reviews (ROBIS) tool (34). ROBIS is useful and reliable for systematic reviewers to identify areas where bias may be introduced into systematic review methods: study eligibility criteria; identification and selection of studies; data collection and study appraisal; and synthesis and findings (34). We will summarize the number of systematic reviews that had a low, high, or unclear concern for each domain and the number of reviews at high or low risk of bias. Risk of bias ratings will be used in the data synthesis process to inform the conclusions of this review. No study will be excluded based on its risk of bias evaluation.

Data synthesis

Based on the data extracted, we will organize information from the reviews about prognostic factors into a comprehensive map. This synthesis will be inspired by the proposed model of Hou et al. (21) which organized the predictors in larger categories of prognostic factors, i.e. predisposing, precipitating, and perpetuating factors. We will also classify the factors regarding International Classification of Functioning, Disability and Health (ICF) (35). We will present data in tabular form and graphically if possible, in order to visually demonstrate the diversity of data in terms of quality of evidence and quality of reviews. We will produce a synthesized list of prognostic factors ranked with consideration of the quality of the evidence, risk of bias, and magnitude of long-term gravity of symptoms. Narrative descriptions from each review will complement the data and provide a comprehensive understanding of the synthesis.

Discussion

There are increasing interests in the population and in the research about mTBI prevention, diagnosis, and prognosis (4, 15, 16, 36). A large body of evidence has emerged concerning the course of this healthcare condition. Multiple systematic reviews synthesized information about this population and many studied prognostic factors associated with persistent symptoms.

To our knowledge, there is no comprehensive systematic mapping or model related to all the prognostic factors of persistent symptoms after mTBI. The results of an OvR (systematic review of systematic reviews) of prognostic factors related to persistent symptoms after mTBI would provide a comprehensive state of evidence in this area. We aim to present a systematic evidence synthesis concerning all factors that affect the risk of persistent symptoms and to describe the level of evidence that supports it. In order to have an organized and usable synthesis, our goal is to include all prognostic factors into categories based on the types of factors found in the literature.

We expect that results of this OvR will help multiple stakeholders, such as clinicians and healthcare managers, to understand the prognosis of their patients and to focus their time and resources on patients needing the most. The results of this overview could also inform decision-makers and policymakers about the challenge of early identification of prognostic factors in order to prevent onset of persistent symptoms.

We anticipate potential limitations for this overview beginning with the variety in the characteristics of the population included in the reviews. Systematic reviews often regroup populations composed of veterans and military personnel and adults with sport-related brain injury. We expect to identify a broad variability of prognostic factors that it could be difficult to synthesize into a single comprehensive model. It is known that overviews of reviews often lack methodological rigor because there are no pre-established reporting guidelines (37). However, we have based our methods on several previous works (22–29) that can appropriately guide us through a rigorous process.

Abbreviations

CINAHL: Cumulative Index to Nursing and Allied Health Literature; ICF: International Classification of Functioning, Disability and Health; mTBI: mild traumatic brain injury; OvR: Overview of systematic reviews; PRISMA(-P): Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Protocol); ROBIS: Risk of bias in systematic review; WHO: World Health Organization

Declarations

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Availability of data and materials

All data generated or analyzed during this study will be included in the published overview article.

Authors' contributions

JD conceptualized the study, was the lead author of the manuscript and is the guarantor of the review. MEL and EDG contributed to concept development, protocol development, and manuscript writing.

Ethics approval and consent to participate

Ethical approval is not required for this study as it is a systematic review.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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