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WHAT IS THE DEFINITION OF SPORTS-RELATED CONCUSSION – A SYSTEMATIC REVIEW

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Short title: definition of concussion

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ABSTRACT

Objectives: Various definitions for concussion have been proposed, each having their strengths and weaknesses. We reviewed and compared current definitions and identified criteria necessary for an operational definition of sports-related concussion (SRC) in preparation of the 5th concussion consensus conference (Berlin, Germany). We also assessed the role of biomechanical studies in informing an operational definition of SRC.

Design: Systematic literature review

Data sources: MEDLINE, Embase, CINAHL, Cochrane-CRCT, SportDiscus (accessed 14/09/2016).

Eligibility criteria for selecting studies: Studies reporting (clinical) criteria for diagnosing SRC and studies containing SRC impact data.

Results: Out of 1601 articles screened, 36 studies were included (2.2%), reporting on criteria for SRC definitions, (14) or biomechanical aspects of concussions (22). Six different operational definitions, focusing on clinical findings and their dynamics were identified. Biomechanical studies were obtained almost exclusively in American football players. Angular and linear head accelerations linked to clinically confirmed concussions demonstrated considerable individual variation.

Summary/conclusions: SRC is a traumatic brain injury that is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces with several common features that help defining its nature. Limitations identified include that current criteria for diagnosing SRC are clinically oriented, and there is no gold/standard to assess their diagnostic properties. A future, more valid definition of SRC would better identify concussed players by demonstrating high predictive positive/negative values. Currently, the use of helmet-based systems to study the biomechanics of SRC is limited to few collision sports. New approaches need to be developed to provide objective markers for SRC.

Bullet statements

What is already known?

- Over the past 50 years, various definitions of sports-related concussion (SRC) and mild traumatic brain injury (mTBI) have been proposed by individual authors, different research groups and international bodies.
- Currently, there is no gold or reference standard for SRC diagnosis, and the diagnostic properties of the various definitions have not been studied.
- The different definitions of SRC do not concur with one another, and this variability has likely caused information or diagnostic misclassification bias in past studies on the management and prognosis of SRC.

What are the new findings?

- Amongst currently available consensus-based definitions of SRC, the consensus statement from the CISG can be considered the opinion leader based on citation statistics.
- These consensus-based definitions, however, showed different levels of detail and weighted distinct domains differently. Limitations even in those definitions that provided additional clarifying statements were demonstrated, including the overlap / distinction between SRC and mTBI.
- Angular and linear head accelerations linked to clinically confirmed SRC demonstrated considerable individual variation.

Key words: head injury, definition, sports, systematic review, biomechanics.

INTRODUCTION

Sports-related concussion (SRC) is a well-recognized clinical entity. However, its pathophysiologic basis remains poorly understood. In the broadest clinical sense, concussion is often defined as representing the immediate and transient symptoms of a mild traumatic brain injury (mTBI). Such operational definitions, however, do not give any insights into the underlying processes through which the brain is impaired, nor do they distinguish different grades of severity, nor reflect insights into the persistence of symptoms and/or abnormalities on specific investigational modalities.

Since the 1970's, clinicians and scientists have begun to distinguish SRC from other causes of concussion and mTBI, such as seen in motor vehicle crashes etc. Whilst this seems like an arbitrary separation from other forms of TBI,^{1,2} it is largely driven by sporting bodies who see the need to have clear and practical guidelines to determine recovery and safe return to play for athletes suffering a SRC. In addition, sports participation can be viewed as research laboratories to study SRC and mTBI, given the detailed SRC phenotype data that is typically available in many sports.³ Having said that, it is critical to understand that the lessons derived from non-sporting mTBI research informs the understanding of SRC (and vice versa) and this arbitrary separation of sporting vs. non-sporting TBI should not be viewed simply as a dichotomous or exclusive view of TBI.

Over the past 50 years, various definitions of concussion and mTBI have been proposed by individual authors, different research groups and international bodies. These definitions, however, do not necessarily concur with one another, although there are a number of common elements. The definitional differences however, make the understanding of injury epidemiology problematic and management challenging.⁴

This systematic review offers an overview of previous concussion definitions and on the role of biomechanical studies in this context. These were specific review questions given to this writing group by the Concussion In Sport Group (CISG). It aims at providing an updated operational definition of concussion and is part of a series of articles written in preparation of the 5th concussion consensus conference held in October 2016 in Berlin, Germany.

HISTORICAL PERSPECTIVE

The clinical manifestations of concussion as a transient neurological syndrome due to head shaking (or "commotion") without structural brain injury have been known since the 10th century AD when the Persian physician, Rhazes first defined the condition.⁵⁻⁷ Following pioneering experimental primate studies demonstrating the transient and functional nature of concussion, the term *acceleration concussion* was proposed as the generic descriptor that should be applied to all forms of traumatic brain injury.⁸ Implicit in this concept is that the term *concussion* should be synonymous with *traumatic brain injury* of all severities. A variation on this view holds that concussion refers to the mechanism of injury and motion of the brain within the skull rather than any clinical symptoms or pathology.⁹

Dating back to the 1930's, numerous anecdotal concussion severity-grading scales have been published reflecting the variety of prevailing theories in existence at the time.^{10,11} By 2001, there were approximately 45 published scales, none of which had been scientifically validated.^{12,13} Whilst not defining concussion per se, these scales broadly attempted to

separate arbitrary levels of concussion severity based on clinical symptoms that would, in turn, inform management and return to play advice. These scales have been reviewed in detail elsewhere; however, it was the view of the Concussion in Sport Group (CISG) in 2001, that these should be abandoned and clinical measures of assessment and recovery be utilised to determine safe return to play.¹²

WHAT DO BIOMECHANICS TELL US ABOUT THE DEFINITION OF SRC?

Studies examining biomechanics and head injury (including TBI) demonstrate broadly that impacts causing SRC are less severe than impacts causing cranial fractures, intracranial haemorrhages and diffuse axonal injury.¹⁴⁻¹⁸

Biomechanical studies of concussion demonstrate both differential effects on brain regions depending upon the impact force, site of impact and bony architecture of the skull; as well as, considerable intrinsic variation in tolerance to head impacts, which will depend on energy status and previous concussion and could be speculated to have a genetic basis as well.¹⁹

Recent studies on SRC, have reported head impact exposure patterns for specific sports, e.g. American football, ice hockey and Australian football. Those studies report head impact characteristics including: frequency, head kinematics, head impact location, and injury outcome. To quantify head impacts, studies have used helmet-based systems, mouthguard/headband/skin sensors as well as videometric studies. The measured or estimated head kinematics provide a starting point to understanding brain tissue loading. Studies have aimed at identifying concussion thresholds for head acceleration (linear and angular).¹⁸ Within these studies, the use of instrumented helmets has provided information on head impact exposures, although there remains some debate regarding the accuracy and precision of these head kinematic measurements.

Biomechanical modeling demonstrates that brain loading patterns (stresses and strains) are not uniformly distributed due to factors including: the brain geometry, brain tissue properties, bony architecture of the internal skull and connective tissue, e.g. falx cerebri and tentorium cerebelli. This means that certain anatomical areas will have greater or lesser physiological or biochemical disturbance depending on the interplay of the external forces, the head's overall kinematic responses and brain sensitivity, such that resultant clinical symptoms may vary from person to person.²⁰⁻²³

To which extent such measurements of head kinematic responses, e.g. linear and angular head acceleration, may influence a definition of concussion, has not been determined and a complete biomechanical understanding of these injuries and related modeling to predict SRC remains a work in progress.²⁴

AIMS OF THE REVIEW

The aim of this review was to perform a systematic review of the literature as per the CISG protocol²⁵ and specifically addresses the following two questions:

- 1) What are the critical clinical criteria for an operational definition of SRC?

2) Do the published biomechanical studies inform us about the definition of SRC?

As per the CISG process, the systematic review was presented at the 5th concussion consensus conference in Berlin, Germany. The updated definition of SRC was developed from the literature review and informed by public discussions and was finalized by the scientific committee.

MATERIALS AND METHODS

The overall methodology of the CISG systematic review process has been outlined in a separate paper published accompanying this review.²⁵

Data sources and searches

A literature search (MEDLINE, Embase, CINAHL, Cochrane Central Register of Clinical Trials (CRCT), SportDiscus) was performed (14/09/2016) to identify English-language articles reporting on clinical criteria of a definition of SRC (aim 1) or on original data of the biomechanics of SRC in humans (aim 2). The MEDLINE (OVID) search strategy was translated for each database, and is reported in supplement 1.

Note that for aim 1 we only included manuscripts that made a significant contribution to the diagnostic criteria for SRC, i.e. modified existing diagnostic criteria or presented new criteria. Manuscripts that referred to, discussed or compared existing definitions of SRC were not eligible. Whilst for aim 1, consensus papers and reviews were also considered; original contributions containing data on players with clinically confirmed SRC were eligible only for aim 2. The role of biomarkers in concussion was addressed in a separate review in this issue and therefore is not further investigated here.

A manual search of reference lists from eligible articles was performed. We did not seek to identify research abstracts from meeting proceedings or unpublished studies. Studies with five or more participants were eligible for aim 2. This review complies with PRISMA guidelines.²⁶

Study selection

All identified articles were subject to title and abstract screening by two independent reviewers (AAT, NFD). Full-text screening was applied to all abstracts considered eligible by at least one reviewer. Articles were selected using pre-determined criteria (for exclusion criteria see supplement 1). Discrepancies in selection status and reasons for exclusion were settled between the two reviewers by discussion and adjunction of a third reviewer (JD) if needed.

/ Figure 1 about here */*

Data extraction and data synthesis

Data extraction was performed by AAT and confirmed by NFD. For aim 1, we extracted the key components of the concussion definition and how the definition was established. Data synthesis in these studies focused on the description of pre-defined key features (symptom onset and duration, mechanism, loss of consciousness, resolution of symptoms and neuroimaging), on the distinction between concussion and mTBI and on the number of

citations. In studies reporting on biomechanical aspects of SRC (aim 2), we extracted key aspects such as the investigated sports, recording devices used, acceleration values resulting in a concussion and concussion location and determined the distribution of mean linear and rotational acceleration values and the mean (± 1 standard deviation (SD)) distribution of head impact location amongst studies.

QUADAS-2 assessment of included studies

For included studies reporting original data on the biomechanics of concussion (aim 2), the risk of bias and applicability concerns were assessed by one reviewer (AAT). A second reviewer (NFD) confirmed ratings, disagreements were resolved by discussion. We opted for the QUADAS-2 tailored study criteria, as they are widely used and recommended for the assessment of diagnostic accuracy studies.²⁷ We did not restrict inclusion further based upon QUADAS-2 results. Note that we did not apply QUADAS-2 to consensus/statement papers providing definitions of concussion (aim 1), as this was not appropriate for this sort of publications.

The QUADAS-2 tool consists of four core domains (patient selection, index test, reference standard, flow/timing).²⁷ Risk of bias is assessed for all four domains, and applicability is assessed for the first three domains. Thus, seven items per study are assessed. For each item the risk of bias is identified as “high”, “low” or “unclear”.

RESULTS

We identified 1601 citations for title/abstract screening and 123 articles for full-text screening. Eventually 36 (2.2%) studies were included for quantitative synthesis (Figure 1). Among the 36 studies included, we identified 14 manuscripts defining the term concussion according to our selection criteria (aim 1), whilst 22 manuscripts reported on biomechanical aspects of SRC (aim 2).

AIM 1: STUDIES REPORTING ON CONCUSSION DEFINITIONS

From the 14 manuscripts focusing on defining the term concussion (Table 1), 12 studies from six different organizations (CISG, American Medical Society for Sports Medicine (AMSSM), National Athletic Trainers' Association (NATA), American Academy of Neurology (AAN), Team physician consensus group (joint statement by the American Academy of Family Physicians, the American Academy of Orthopaedic Surgeons, the American College of Sports Medicine, the American Medical Society for Sports Medicine, the American Orthopaedic Society for Sports Medicine, and the American Osteopathic Academy of Sports Medicine), Committee on head injury nomenclature from the Congress of Neurological Surgeons) provided consensus-based operational definitions of concussion.^{12 28-37} One study provided original data about the implementation of a structured concussion assessment in a paediatric emergency department (ED),³⁸ and one study reviewed definitions of concussion as provided on web sites.³⁹

/* Table 1 about here */

Comparison of the different consensus-based operational definitions identified

Key aspects of the six definitions included are provided in Table 2. Whilst all but one definition³⁷ were proposed or revised within the last five years and were restricted to SRC, they differed in the level of detail and the domains addressed.

/* Table 2 about here */

Comparing key elements characterizing a concussion in the proposed consensus-based definitions showed both similarities and discrepancies for some items (Table 2). Whilst in all definitions loss of consciousness (LOC) was considered optional for making the diagnosis, onset (immediate/rapid/within minutes), duration, mechanism of impairment, and resolution were addressed only by some of the definitions (Table 2).

The assessment of specific domains was described in four definitions. Clinical symptoms typically included physical, cognitive, emotional and sleep disturbances, whilst examination included physical signs and neurocognitive testing (for cognitive and neurobehavioural alterations). A statement regarding typical findings on standard structural neuroimaging was provided only by two groups (CISG and team physician consensus).

The terms "concussion" and "mTBI" were handled differently in these consensus statements.^{30-33 36} Whilst concussion was considered a subset of TBI (CISG)³⁰ or mTBI (AMSSM),³¹ concussion and mTBI were used synonymously by others (Team physician consensus statement, AAN consensus, NATA).^{32 33 36}

AIM 2: STUDIES REPORTING ON BIOMECHANICAL ASPECTS OF CONCUSSION

Twenty-two manuscripts reporting on biomechanical aspects of SRC met our inclusion criteria. From two studies, results were reported in more than one paper. For each study we considered only the most recent publication^{40 41} and did not include the others.^{22 24 42} From the remaining 19 manuscripts key aspects were extracted (Tables 3 and 4).

Risk of bias assessment (QUADAS-2)

Risk of bias and applicability concerns for patient selection were rated as "high" in 6 studies as only a subset of identified concussions were included (supplementary file 2). For index testing all studies were considered "high" risk of bias as the biomechanical data were analyzed and interpreted with the knowledge of the results from the reference test. Eleven studies that were either directly funded by or had one/several co-author(s) who had a vested financial interest in the accelerometry system used, were rated as "high" risk for applicability concerns of the index test. Regarding the reference standard, we considered all 22 studies as "unclear" risk of bias, as it remains unknown if all concussions were identified by the medical staff.

/* Table 3 about here */

Key findings of included studies

To quantify head impacts, 17/19 studies used helmet-based systems. The Head Impact Telemetry System (HITS) was used in 15 studies and instrumented mouthguards with 6-DOF sensors were used in 2 studies. Video-analysis was applied to a study cohort of rugby and Australian rules football players,²¹ providing more detailed analysis on a subset of players in a follow-up study.⁴¹ Different combinations of parameters were assessed in these studies. The methods by which concussions were diagnosed remained unclear in five studies and only five studies adhered to published concussion consensus definitions.

/* Table 4 about here */

Measured mean peak linear accelerations in concussed players (data from 13/15 studies using the HITS) ranged between 43.0 and 145.0g. In-between these boundaries, most studies reported mean peak linear acceleration values of approximately 100g. For rotational acceleration, mean peak values (n=9 studies) in concussed players ranged between 3,620 and 7,230rad/s² (Table 4). Results from studies using instrumented mouthguards or video-based analyses demonstrated a similar range for peak linear accelerations, whilst peak rotational accelerations tended to be higher (Table 4).

Eight HITS-based studies in American football players (and ice hockey players in one of those studies) reported the location of head impacts (n=308), with frontal impacts identified most frequently (n=151; 49%). In a single study on head impact location in Australian rules football and rugby based on video-analysis,²¹ 69% of impacts were located on the side of the head. In a follow up study including non-injured athletes, the proportion of impacts to the temporal region was significantly greater (p=0.05) for concussion cases compared to no-injury cases, 60–23%, respectively.⁴¹ It is important to recognize that structural TBI or cranial fractures did not occur in these studies and the vast majority of head impacts recorded with the HIT system did not result in concussion; e.g. approximately 0.02% of the impacts in Broglio et al. 2011⁴³ were associated with a diagnosis of concussion.

In summary, reported peak linear and rotational acceleration values in players with clinically confirmed concussion showed large inter-individual variability and cut-off values were proposed in a single study only. Noteworthy, all studies had a high risk of bias and a high risk for applicability concerns for at least one item, warranting caution in interpreting these studies.

DISCUSSION

Our review identified six consensus-based definitions of SRC. Amongst the different organizations providing definitions, the consensus statements from the CISG were cited most frequently (with 1376 citations in Google Scholar for the 2009 consensus statement), followed by the statements from AAN, NATA and AMSSM (all around 500-700 citations). Since the 1966 Statement of the Congress of Neurological Surgeons was issued prior to the recent popularity of this topic, the number of citations for this document must be interpreted with caution.

/* Table 5 about here */

Based on the highest number of citations, the consensus statements from the CISG can be considered the opinion leader although it is acknowledged that earlier definitions largely predate the era of internet citations.^{12 28-30}. These consensus-based definitions showed different levels of detail and weighted distinct domains differently. We demonstrated limitations even in those definitions that provided additional clarifying statements.^{30 36}

Recommendations for a future operational definition of SRC

Based on this systematic review as well as consensus discussions, it is recommended that the key elements of a future **clinical or operational definition of SRC** ideally includes some or all of the following elements:

- Biomechanics – the injury is caused by quantified direct or indirect force(s) to the brain.
- Physiology - a defined physiological disruption of brain function.
- Clinical - a range of evolving clinical symptoms and signs including an alteration in cognitive functioning or mental state (e.g. confusion, disorientation, slowed thinking) that may or may not involve transient loss of consciousness.
- Neuroimaging – a defined abnormality on advanced imaging platforms reflecting the underlying physiological abnormalities and clinical features.
- Fluid biomarkers and genetics – defined abnormalities reflecting the underlying physiological disruption or injury

Despite many publications and definitional attempts, these considerations leave several issues unanswered, notably: does being dazed, seeing stars or feeling dizzy in the absence of altered mental state constitute either concussion or mTBI? The definition also does not explain how known concussion modifiers influence the clinical presentation.

Berlin consensus definition of sports-related concussions

The 2016 Berlin consensus conference operational definition (“Berlin definition”) is presented below. This definition is based on the systematic review of the literature presented here as well as the consensus discussions during the plenary session by the conference participants and the expert panel.

Concussion is a traumatic brain injury induced by biomechanical forces. Several common features that may be utilized in clinically defining the nature of a concussive head injury include...

- *Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an impulsive force transmitted to the head.*
- *Concussion typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, signs and symptoms evolve over a number of minutes to hours.*
- *Concussion may result in neuropathological changes, but the acute clinical signs and symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.*

- *Concussion results in a range of clinical signs and symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive features typically follows a sequential course. However, in some cases symptoms may be prolonged.*

The clinical signs and symptoms of concussion cannot be explained by drug, alcohol, medication use, other injuries (such as cervical injuries, peripheral vestibular dysfunction etc.), or other comorbidities (e.g. psychological factors or coexisting medical conditions etc).

Limitations and outlook

Our systematic review may have a potential publication bias and language bias as only published, English-language articles were considered. It is important to note that even if a healthcare professional is “skilled”, what reproducible and valid criteria do they use to make this “diagnosis” of SRC? Thus, the major challenges in concussion diagnosis are:

1. There is no gold or reference standard measure of concussion.
2. There is marked variability in the diagnostic criteria with no studies examining the measurement properties of the definitional criteria.
3. Given 1 and 2, there is likely a large amount of information bias inherent in all concussion studies because there is no validated case definition. Thus, information bias would be present in studies of risk, prevention, prognosis, intervention and long-term sequelae. This likely explains some of the variability of findings in these areas.

The challenge is to validate an operational definition of SRC based on clinical criteria until a “proven” gold standard is discovered and validated. This is highlighted as a major area of research for the reasons outlined above. If an objective gold standard becomes available, the clinical criteria could then be tested against it to provide diagnostic metrics such as positive and negative predictive values and likelihood ratios. Another approach in the absence of an objective gold standard is to use the prognostic utility of a concussion definition. If it accurately predicts outcome, it could be a useful measure to identify and triage cases. Such a prediction rule would be more useful than a diagnosis based on unknown criteria.⁴⁴

Currently, the investigation of biomechanical aspects of SRC focuses on high school / college collision sports where players wear helmets. Whilst in these studies peak linear acceleration values in concussed players averaged approximately 100g, this is in good agreement with a recent systematic review.¹⁸ These impacts are less severe than head impacts resulting in structural head injury, e.g. intracranial haemorrhages or contusions, diffuse axonal injury, and cranial fractures.^{15-17 45} Methodological limitations in these studies must be considered, such as helmet fit, not using consensus-based concussion definitions and not reporting whether the diagnosis was made by skilled medical personal or not. Furthermore, lack of duplicate risk of bias assessment in our systematic review should be considered as a limitation. Developments are occurring in mini-accelerometer devices that can be worn by athletes who do not wear a helmet. These devices offer opportunities for research and clinical practice. At present, there is no evidence that accelerometer devices or video-based observations of athletes can provide a ‘diagnosis’ of concussion. Therefore, at present head acceleration data should not be used in isolation to remove a player from play or allow a player to keep playing following a hit.

CONCLUSIONS

With regards to both aims addressed in this systematic review, newer technological advances may give important insights into the underlying pathophysiology and ultimately provide a platform to develop a clear definition in the future. It can be anticipated that, in the future, head injury and concussion may eventually be defined by the severity of clinical signs, as well as genetic, epigenetic, metabolomic, proteomic, advanced imaging findings and blood/CSF biomarkers.

REQUIRED STATEMENTS

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Conflict of interest:

Dr. McCrory: Paul McCrory is a co-investigator, collaborator, or consultant on grants relating to mild TBI funded by several governmental organizations. He is directly employed by the National Health & Medical Research Council of Australia and is based at the Florey Institute of Neuroscience and Mental Health. He is Co-Chair of the Australian Centre for Research into Sports Injury and its Prevention (ACRISP), which is one of the International University Research Centres for Prevention of Injury and Protection of Athlete Health supported by the International Olympic Committee (IOC). He is co-chair of the International Concussion in Sport Group. He has a clinical and consulting practice in general and sports neurology. He receives book royalties from McGraw-Hill and was employed in an editorial capacity by the British Medical Journal Publishing Group from 2001 to 2008. He has been reimbursed by the government, professional scientific bodies, and sporting bodies for travel costs related to presenting research on mild TBI and sport-related concussion at meetings, scientific conferences, and symposiums. He received consultancy fees in 2010 from Axon Sports (US) for the development of educational material (which was not renewed) and has received research funding since 2001 from CogState Inc. He has not received any research funding, salary or other monies from the Australian Football League, FIFA or the National Football League. The Australian Football League funds research at the Florey Institute under a legal memorandum and Dr. McCrory does not receive any money from this industry funded research. Dr. McCrory is a cofounder and shareholder in two biomedical companies (involved in eHealth and Compression garment technologies) but does not hold any individual shares in any company related to concussion or brain injury assessment or technology. He did not receive any form of financial support directly related to this manuscript.

Dr. Feddermann-Demont reports no conflict of interest.

Prof. Dvorak reports no conflict of interest

Dr. McIntosh is a self-employed consultant and holds honorary academic appointments. He has been funded as a consultant to undertake research and policy related work for government, sports federations and industry on the topic of safety and injury risk management, including concussion, head injury and helmets. He did not receive any form of financial support directly related to this manuscript. He reports no conflicts of interest.

Dr. Vos is a neurologist and Chairman of the Steering Committee of a trial in traumatic brain injury sponsored by EVER Neuro Pharma GmbH. He has been funded as a consultant for EVER Neuro Pharma. He did not receive any form of financial support directly related to this manuscript. He reports no conflicts of interest.

Dr. Cassidy is an injury epidemiologist employed by the University Health Network, University of Toronto. He is a professor in the Division of Epidemiology and the Institute of Health Policy, Management and Evaluation at the Dalla Lana School of Public Health, University of Toronto. He has received funding from the Ontario Neurotrauma Foundation to undertake systematic reviews on mild traumatic brain injury and served on the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury, which received funding from various sources, including traffic insurance companies in North America and Europe. He was retained as an expert witness for the National Hockey League on November 30, 2016. He did not receive any form of financial support related to this manuscript, and has no other conflicts of interest to report.

Dr. Echemendia is a consultant to the National Hockey League, Major League Soccer, US Soccer Federation, and Princeton University. He receives financial remuneration for these consulting relationships. He has a clinical practice in sport neuropsychology and serves as an expert (neuropsychology, sport neuropsychology) in medico-legal cases involving traumatic brain injury.

Dr. Willem Meeuwisse, MD, PhD is the Medical Director of the National Hockey League. He has received research grant support through the University of Calgary from the Canadian Institutes of Health Research, Alberta Innovates Health Solutions, the International Football Association (FIFA), Alberta Children's Hospital Research Institute and the Hotchkiss Brain Institute. He is the founding Chair of the Sport Injury Prevention Research Centre, which is one of the International Research Centres for Prevention of Injury and Protection of Athlete Health supported by the International Olympic Committee (IOC). He has a clinical consulting practice in sport medicine at the University of Calgary Sport Medicine Centre. He is an Expert Group member of the IOC Medical Commission and has received travel funding in that capacity. He did not receive any form of financial support directly related to this manuscript and has no conflicts of interest to report.

Dr. Tarnutzer reports no conflict of interest.

TABLES

Table 1: Overview of included studies providing definitions of concussion*

Authors, year published	Responsible organization	Type of manuscript	Restricted to sport concussion (yes/no)	Age group	Concussion grading system (yes/no)	Remarks
Congress of Neurological Surgeons 1966 ³⁷	Committee on head injury nomenclature	Consensus statement	no	All ages	No	
Kelly et al. 1997 ⁴⁶	American Academy of Neurology	Consensus statement	Yes	All ages	Yes (mild / moderate / severe)	
Giza et al. 2013 ³²	American Academy of Neurology	Consensus statement	Yes	All ages	No	Revision of 1997 AAN consensus ⁴⁶
Aubry et al. 2002 ¹²	CISG	Consensus statement	Yes	All ages	No	
McCroory et al. 2005 ²⁸	CISG	Consensus statement	Yes	All ages	No	Revision of the 2002 consensus ¹²
McCroory et al. 2009 ²⁹	CISG	Consensus statement	Yes	All ages	No	Revision of the 2005 CISG consensus ²⁸
McCroory et al. 2013 ³⁰	CISG	Consensus statement	Yes	All ages	No	Revision of the 2009 CISG consensus ²⁹
Guskiewicz et al. 2004 ³⁴	National Athletic Trainers' Association	Consensus statement	Yes	All ages	No	Existing grading systems are reviewed ^{46 47}
Broglio et al. 2014 ³³	National Athletic Trainers' Association	Consensus statement	Yes	All ages	No	Revision of 2004 NATA consensus ³⁴
Herring et al. 2006 ³⁵	Team physician consensus statement (AAFP, AAOS, ACSM, AMSSM, AOSSM, AOASM)	Consensus statement	Yes	All ages	No	
Herring et al. 2011 ³⁶	Team physician consensus statement (AAFP, AAOS, ACSM, AMSSM, AOSSM, AOASM)	Consensus statement	Yes	All ages	No	Revision of 2006 Team physician consensus ³⁵
Harmon et al. 2013 ³¹	American Medical Society for Sports Medicine	Consensus statement	Yes	All ages	No	
Berg et al. 2014 ³⁹	NA	Original research (retrospective)	Yes	All ages	No	Analysis of concussion definitions on popular concussion-related websites
Boutis et al. 2015 ³⁸	NA	Original research (prospective)	no	Children (5-18y)	No	Implementation of CISG concussion definition in pediatric ED.

Abbreviations: AAFP=American Academy of Family Physicians; AAN=American Academy of Neurology; AAOS=American Academy of Orthopaedic Surgeons; ACSM=American College of Sports Medicine; AMSSM=American Medical Society for Sports Medicine; AOSSM=American Orthopaedic Society for Sports Medicine; AOASM=American Osteopathic Academy of Sports Medicine; CDC=Centers for Disease Control and Prevention; CISG=concussion in sports group; ED=emergency department; NA=not available; NATA=National Athletic Trainers' Association;

* Studies are presented according to the number of citations in Google Scholar (in descending order)

† Accessed on October 19th 2016 (google.scholar.com)

‡ Service provided by Web of Science, Thomson Reuters. Accessed on October 19th 2016.

Table 2: Key components for identifying a concussion – comparison of different definitions*

Organization, year published	Definition of concussion	Domains assessed	Key features	Definition mTBI? Link concussion - TBI?	Notes
Concussion in sports group ¹² 28-30 2002, 2005, 2009, 2013	"A complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces' that 'may be caused by a direct blow to the head, face, neck or elsewhere in the body with an impulsive force transmitted to the head." <u>Common features include:</u> <ul style="list-style-type: none"> • Rapid onset of short-lived impairment of neurological function that resolves spontaneously • May result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury. • Graded set of neurological syndromes that may or may not involve an LOC. Resolution of the clinical and cognitive features typically follows a sequential course. In some cases symptoms may be prolonged. • Typically associated with grossly normal structural neuroimaging studies 	<ul style="list-style-type: none"> • Clinical symptoms (physical, cognitive, emotional) • Physical signs • Cognitive impairment • Neurobehavioral features • Sleep disturbances 	Onset: rapid. Duration: short-lived. Mechanism of impairment: functional disturbance rather than structural injury. LOC: may or may not. Resolution: sequential. Neuroimaging: no abnormalities on standard structural neuroimaging	No (concussion is considered as subset of TBI)	This definition also comments on typical neuroimaging feature in concussion
American Medical Society for Sports Medicine ³¹ 2013	"A concussion is defined as a traumatically induced transient disturbance of brain function and is caused by a complex patho-physiological process. Concussions have also been referred to as mild traumatic brain injuries (mTBI). While all concussions are mTBIs, not all mTBIs are concussions. Concussions are a subset of mTBIs, on the less-severe end of the brain injury spectrum and are generally self-limited in duration and resolution"	<ul style="list-style-type: none"> • Symptoms and signs (physical, cognitive, emotional, sleep) 	Onset: not specified. Duration: transient, self-limited. Mechanism of impairment: functional disturbance. LOC: may or may not. Resolution: not specified Neuroimaging: not specified	No (concussion is considered as subset of mTBI)	
National Athletic Trainers' Association ³³ ³⁴ 2004, 2014	"Trauma- induced alteration in mental status that may or may not involve loss of consciousness"	<ul style="list-style-type: none"> • Not specified 	Onset: not specified. Duration: not specified. Mechanism of impairment: not specified. LOC: may or may not. Resolution: not specified Neuroimaging: not specified	No (concussion and mTBI are used interchangeably)	
American Academy of Neurology ^{32 46}	"Concussion is a trauma-induced alteration in mental status that may or may not involve loss of consciousness. Confusion and amnesia are the hallmarks of concussion. The confusional episode and amnesia may occur immediately	<ul style="list-style-type: none"> • Clinical symptoms (physical, cognitive, emotional) 	Onset: immediate or within minutes. Duration: not specified.	No (concussion and mTBI are used)	1997 definition was used as the 2013 revision provided a

1997, 2013	after the blow to the head or several minutes later"	<ul style="list-style-type: none"> • Physical signs • Cognitive impairment • Sleep disturbances 	Mechanism of impairment: not specified. LOC: may or may not. Resolution: not specified Neuroimaging: not specified	interchangeably)	shortened definition only
Team physician consensus statements (AAFP, AAOS, ACSM, AMSSM, AOSSM, AOASM) ^{35 36} 2006, 2011	<p>"Concussion or mild traumatic brain injury (mTBI) is a pathophysiological process affecting the brain induced by direct or indirect biomechanical forces"</p> <p><u>Common features include:</u></p> <ul style="list-style-type: none"> • Rapid onset of usually short-lived neurological impairment, which typically resolves spontaneously. • Acute clinical symptoms that usually reflect a functional disturbance rather than structural injury. • A range of clinical symptoms that may or may not involve loss of consciousness (LOC). • Routine neuroimaging studies are typically normal. 	<ul style="list-style-type: none"> • Clinical symptoms and signs (cognitive, somatic, affective, sleep disturbances) 	Onset: rapid. Duration: short-lived. Mechanism of impairment: functional disturbance rather than structural injury. LOC: may or may not. Resolution: spontaneous. Neuroimaging: no abnormalities on standard structural neuroimaging	Combined definition for mTBI and concussion	This definition also comments on typical neuroimaging features in concussion
Congress of Neurological Surgeons ³⁷ 1966	"...a clinical syndrome characterized by the immediate and transient post-traumatic impairment of neural function such as alteration of consciousness, disturbance of vision or equilibrium due to mechanical forces."	<ul style="list-style-type: none"> • Not specified 	Onset: immediate. Duration: transient. Mechanism of impairment: not specified. LOC: may or may not. Resolution: not specified Neuroimaging: not specified	Not specified	

Abbreviations: LOC=loss of consciousness. NA=not available

* In case of revised concussion definitions from the same group, the most recent version was considered if not stated otherwise.

Table 3: Overview of included original publications reporting on biomechanical aspects of concussion*

Authors / year published	Times cited (Google)†	Times cited (Web of Science)‡	Study design	Investigated sports	Level of play	Players (n), age, gender (F/M/B)	Recording system	Impacts / concussions	Parameters assessed	Concussion definition used	Diagnosed by	Notes
Duma et al. 2005 ⁴⁸	250	144	Prospective, observational	American football	College	38, NR, M	HITS	3312 / 1	Linear / rotational acc, Δ head vel. GSI, HIC	NR	NR	
Guskiewicz et al. 2007 ²⁰	248	145	Prospective, observational	American football	College	88, 20.2 \pm 1.8y, M	HITS	104714 / 13	Linear / rotational acc	own definition	Team physician	
Greenwald et al. 2008 ⁴⁹	245	158	Prospective, observational	American football	NCAA division I schools / high schools	449, NR, M	HITS	289916 / 17	Linear / rotational acc, GSI, HIC	AAN	Medical staff (not specified)	
Rowson et al. 2012 ⁵⁰	163	85	Prospective, observational	American football	College	335, NR, M	HITS (n=314); custom 6DOF sensors (n=21)	301034 / 57	Rotational acc	CISG	Medical staff (not specified)	
Broglio et al. 2010 ⁵¹	139	79	Prospective, observational	American football	High school	78, 16.7 \pm 0.8y, M	HITS	54247 / 13	Linear / rotational acc,	AAN	Certified AT, physician	
Schnebel et al. 2007 ⁵²	136	79	Prospective, observational	American football	College / high school	56, NR, M	HITS	54154 / 6	Linear acc	NR	NR	
McIntosh et al. 2000 ²¹	100	72	Retrospective	Rugby, Australian rules football	Professionals	100, NR, M	Video	100 / 100	Head impact dynamics		NR	
Brolinson et al. 2006 ⁵³	92	NA	Prospective, observational	American football	College	52, NR, M	HITS	11604 / 3	Linear acc	NR	Medical staff (not specified)	
McAllister et al. 2012 ⁵⁴	76	45	Prospective, observational	American football, ice hockey	College / high school	10, NR, M	HITS	10 / 10	Linear / rotational acc	Own definition	Certified AT, physician	
Funk et al. 2012 ⁵⁵	72	37	Prospective, observational	American football	College	98, NR, M	HITS	37128 / 4	Linear acc, HIC	NR	AT, physician	
Duhaime et al. 2012 ⁵⁶	59	35	Prospective, observational	American football, ice	College	450, NR, B	HITS	486594 / 48	Linear / rotational acc	NR	Certified AT, physician	

				hockey								
Broglio et al. 2011 ⁴³	45	27	Prospective, observational	American football	High school	95, NR, M	HITS	102218 / 20	Linear / rotational acc, HITsp	AAN	Certified AT, physician	
Beckwith et al. 2013 ⁴⁰	39	24	Prospective, observational	American football	College / high school	1208, NR, M	HITS	161732 / 105	Linear / rotational acc, Δ head vel. GSI, HIC	NR	AT, physician	This dataset has previously been reported by Beckwith et al. 2013. ⁴² To avoid duplicity, this study has been removed from the analysis.
Duma and Rowson 2009 ⁵⁷	26	5	Prospective, observational	American football	College	NR, NR, M	HITS	71300 / 6	Linear acc	NR	Team physician	
King et al. 2015 ⁵⁸	23	8	Prospective, observational	Rugby	Amateur	38, 22 \pm 4y, M	Instrumented mouthgard (custom-built 6DOF sensor)	20689 / 2	Linear / rotational acc	NR	Medical staff (not specified)	
McIntosh et al. 2014 ⁴¹	19	4	Prospective, observational	Rugby and Australian rules football	Professionals	40, NR, M	Rigid body simulations, data from video	40 / 27	Linear / rotational acc	NR	NR	The 27 cases with concussion were taken from a larger sample previously published. ²¹ Preliminary analyses of the 27 cases were provided by Frechede and McIntosh 2009 ²⁴ and Patton et al. 2013 ²² .
Hernandez et al. 2015 ⁵⁹	17	4	Prospective, observational	American football, boxing, MMA	College / professional	33, NR, B	Custum 6DOF acc device	513 / 2	18 different parameters	NR	NR	
Wilcox et al. 2015 ⁶⁰	7	4	Prospective, observational	Ice hockey	College	58, NR, F	HITS	NR / 9	Linear / rotational acc, HITsp	Own definition	Certified AT, physician	
Beckwith et al. 2009 ⁶¹	6	NA	Prospective, observational	American football	College / high school	52, 18.9 \pm 2.3y, M	HITS	71390 / 52	Linear / rotational GSI, HIC15	AAN	Medical staff (not specified)	While this study included 901 players, this manuscript only reports on the 52 players with concussion.

Abbreviations: AAN=American Academy of Neurology; acc=acceleration; AT=athletic trainer; B=both gender; CISG=Concussion in Sports Group; DOF=degrees of freedom; F=females; GSI=Gadd Severity Index; HIC=Head Injury Criterion; HITS=Head Impact Telemetry System; HITsp=Head Impact Technology severity profile; M=males; MMA=mixed martial arts; NA=not available; NR=not reported;

* Studies are presented according to the number of citations in Google Scholar (in descending order)

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§ Detailed numbers on the 48 concussions recorded: American football (n=40), women's ice hockey (n=7), men's ice hockey (n=1).

Table 4: Key aspects of studies reporting on the biomechanics of concussion (only studies using HITS).

Authors / year published	Sports investigated	Impacts on days with concussion (mean±1SD, range)	Mean peak values in concussed players (±1SD, range)		Location of head impact (n)				
			Linear acc (g)	Rotational acc (rad/s ²)	Front	Top	Side	Back	All
<u>HIT systems technology used for data acquisition (n=15)</u>									
Duma et al. 2005 ⁴⁸	American football	NR	81.0 (NR)	NR	0	0	1	0	1
Guskiewicz et al. 2007 ²⁰	American football	NR	102.8 ± 30.7 (60.51–168.71)	5,312 ± 3,950 (NR)	NR	NR	NR	NR	13
Greenwald et al. 2008 ⁴⁹	American football	NR	NR	NR	8	3	5	1	17
Rowson et al. 2012 ⁵⁰	American football	NR	NR	5,022 ± 1,791 (NR)	33 (incl. back)	17	7	Pooled with front	57
Broglio et al. 2010 ⁵¹	American football	NR	105 ± 18 (NR)	7,230 ± 1,158 (NR)	8	2	2	1	13
Schnebel et al. 2007 ⁵²	American football	34 ± 24 (NR)	127.0 ± 25.5 (81.9 – 145.7)	NR	NR	NR	NR	NR	6
Brolinson et al. 2006 ⁵³	American football	NR	103.3 ± 42.3 (NR)	NR	1	0	1	1	3
McAllister et al. 2012 ⁵⁴	American football, ice hockey	NR	73.6 ± 21.3 (NR)	5,025 ± 1,226 (NR)	NR	NR	NR	NR	10
Funk et al. 2012 ⁵⁵	American football	NR	145 ± 35 (NR)	NR	NR	NR	NR	NR	4
Duhaime et al. 2012 ⁵⁶	American football, ice hockey	19.5 ± 15.7 (NR)	86.1 ± 42.6 (16.5–177.9)*	3,620 ± 2,166 (183–7,589)*	13	9	5	8	35
Broglio et al. 2011 ⁴³	American football	25.0 ± 18.3 (NR)	93.6 ± 27.5 (NR)	6,402.6 ± 1,753.9 (NR)	11	3	5	1	20
Beckwith et al. 2013 ⁴⁰	American football	25.8 ± 22.7 (1 - 108)	102.5 ± 33.8 (29.3 – 205.3)	3,977 ± 2,272 (183 – 10,484)	48	26	17	14	105
Duma and Rowson 2009 ⁵⁷	American football	NR	132.3 ± 49.8 (NR)	NR	NR	NR	NR	NR	6
Wilcox et al. 2015 ⁶⁰	Ice hockey	NR	43.0 ± 11.5 (NR)	4,030 ± 1,435 (NR)	NR	NR	NR	NR	9
Beckwith et al. 2009 ⁶¹	American football	NR	107 ± 31 (NR)	7,079 ± 3,408 (NR)	28	12	11	4	55
All studies					151 (49.0)	73 (23.7)	54 (17.5)	30 (9.7)	350
<u>Instrumented mouthguard with custom-built 6DOF sensor used for data acquisition (n=2)</u>									
King et al. 2014 ⁵⁸	Rugby	NR	74.9 ± 28.2 (NR)	7627.5 ± 3263.6 (NR)	NR	NR	NR	NR	2
Hernandez et al. 2015 ⁵⁹	American football, boxing, MMA	NR	95.5 ± 14.8 (85 – 106)	9565 ± 3571 (7040 – 12090)	NR	NR	NR	NR	2
<u>Video-based analyses (n=1)</u>									
McIntosh et al. 2000 ²¹	Rugby, Australian rules football	NR	NR	NR	19†	0	67	11	97‡
McIntosh et al. 2014 ⁴¹	Rugby, Australian rules football	NR	103.4 ± 29.5 (NR)	7,951 ± 3,562 (NR)	7§	0	18	2	27¶

* Calculations based on those 31 concussions with an identified single impact leading to symptoms. For impact location, 35 concussions were considered.

† This includes 9 concussions to the face.

‡ Impact location was not reported in 3 players.

§ This includes 3 concussions to the face.

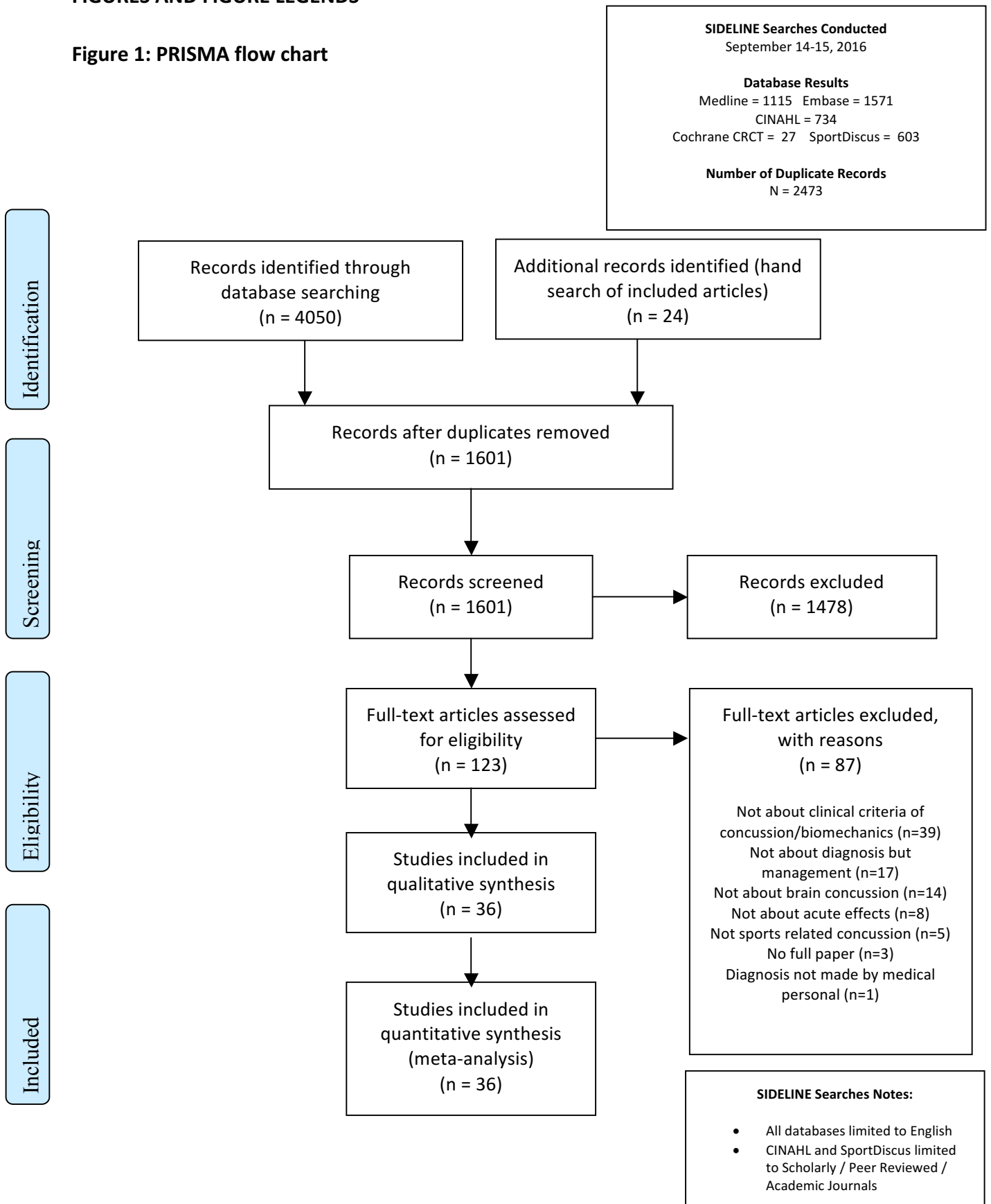
¶ This study provides a more detailed analysis of the biomechanical aspects in a subset of concussed players previously published.²¹ Note that the impact location has already been reported by the previous study.

Table 5: number of citations for individual studies.

Authors, year published	Responsible organization	Times cited (Google)†	Times cited (Web of Science)‡
McCrory et al. 2009 ²⁹	CISG	1376	203
McCrory et al. 2013 ³⁰	CISG	1158	468
McCrory et al. 2005 ²⁸	CISG	848	383
Aubry et al. 2002 ¹²	CISG	826	180
Harmon et al. 2013 ³¹	American Medical Society for Sports Medicine	532	186
Guskiewicz et al. 2004 ³⁴	National Athletic Trainers' Association	513	269
Giza et al. 2013 ³²	American Academy of Neurology	374	192
Kelly et al. 1997 ⁴⁶	American Academy of Neurology	352	379
Broglio et al. 2014 ³³	National Athletic Trainers' Association	140	66
Herring et al. 2011 ³⁶	Team physician consensus statement (AAFP, AAOS, ACSM, AMSSM, AOSSM, AOASM)	109	0
Boutis et al. 2015 ³⁸	NA	6	2
Herring et al. 2006 ³⁵	Team physician consensus statement (AAFP, AAOS, ACSM, AMSSM, AOSSM, AOASM)	4	1
Berg et al. 2014 ³⁹	NA	3	0
Congress of Neurological Surgeons 1966 ³⁷	Committee on head injury nomenclature	NA	39

FIGURES AND FIGURE LEGENDS

Figure 1: PRISMA flow chart



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Supplementary file 1: Detailed search and selection strategy

The search strategy was designed by Dr. K. A. Hayden. We searched five databases (MEDLINE, Embase, CINAHL, Cochrane CRCT, SportDiscus) for English-language articles. For MEDLINE, the following search strategy was used. This search strategy was then translated for each database.

Database(s): Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:

Searches

- 1 exp Brain Concussion/
- 2 mild concussion*.tw.
- 3 cerebral concussion*.tw.
- 4 concussion*.tw.
- 5 mild traumatic brain injur*.tw.
- 6 mtbi.tw.
- 7 sport* related concussion*.tw.
- 8 commotio cerebri.tw.
- 9 or/1-8
- 10 biomechanic*.tw.
- 11 clinical*.tw.
- 12 objective*.tw.
- 13 scientific*.tw.
- 14 operational.tw.
- 15 physiologic*.tw.
- 16 or/10-15
- 17 characteristic*.tw.
- 18 criteria*.tw.
- 19 symptom*.tw.
- 20 component*.tw.
- 21 evaluation*.tw.
- 22 diagnos*.tw.
- 23 definition*.tw.
- 24 define.tw.
- 25 changes.tw.
- 26 exp Classification/
- 27 classification*.tw.
- 28 "Concept Formation"/
- 29 or/17-28
- 30 exp Sports/
- 31 exp Snow Sports/ or exp Racquet Sports/
- 32 exp Athletes/
- 33 exp Hockey/ or exp Soccer/ or exp Football/

34 (Sport* or athlete* or athletic* or player* or team* or competitor* or jockey* or varsity).tw.

35 (Soccer or football or rugby or baseball or basketball or boxing or hockey or volleyball or netball or diving or racquet* or martial arts or equestrian or lacrosse or skating or skiing or snowboard* or wrestling or softball).tw.

36 or/30-35

37 9 and 16 and 29 and 36

38 limit 37 to english language

39 limit 38 to (addresses or autobiography or bibliography or biography or directory or editorial or in vitro or interactive tutorial or interview or lectures or legal cases or legislation or letter or news or newspaper article or patient education handout or periodical index or personal narratives or portraits or video-audio media or webcasts)

40 38 not 39

Our search was updated through September 14, 2016. We also performed a manual search of reference lists from eligible articles. Research abstracts from meeting proceedings or unpublished studies or non-English language studies were not considered. Where appropriate, we attempted to contact authors regarding study details. There was no review protocol.

All identified articles were subject to title and abstract screening by two independent reviewers (AAT, NFD). Articles were selected using pre-determined criteria. Reviewers *excluded* papers that were no full manuscripts (e.g. letters to the editor or correspondence on published studies), did not report on sports-associated head-injuries meeting the criteria for brain concussion or MTBI in athletes, did not focus on the diagnosis of concussion (but e.g. rather on its management) and acute effects of concussion (e.g. on concussion therapy, prognosis, return to play), did not contain data about a) the clinical criteria of a definition of concussion (for example only epidemiological data about concussion frequency) or b) about the biomechanics of concussion in humans, did not require the diagnosis of concussion being made by medical personal (e.g. physician, trained coach, physiotherapist) or reported on less than five cases. Note that studies reporting no original data (e.g. conference consensus statements) were eligible for the assessment of clinical criteria of a definition of concussion as well.

Full-text screening was applied to all abstracts considered eligible by at least one reviewer (i.e., labeled “yes” or “maybe” in the abstract review). The two independent reviewers (AAT, NFD) identified whether full-text manuscripts were eligible and provided a reason for exclusion. Discrepancies in selection status and reasons for exclusion were settled between the two reviewers by discussion and adjunction of a third reviewer if needed.

Information abstracted from each article included study type and publication date, addressed sports, proposed clinical criteria for a definition of concussion and number of citations for aim 1. For aim 2 (biomechanical studies) abstracted information included the investigated sports, level of play, recording systems used and recorded linear/rotational accelerations in concussed players. Data were handled in EndNote X 7.5 (Thomson Reuters, NY) and Microsoft Excel 2011 (Redmond, WA).

Search Results

Our search identified 1601 unique citations, of which 1478 (92.3%) were excluded at the abstract level (see flow diagram in main manuscript for details in the search strategy).

We did not require concordance on the reasons for abstract exclusion, but, of concordant codings (89.2%, n=1319), exclusions were for the following reasons: 37% were not about acute effects of concussion; 28% were not about clinical criteria of concussion or about biomechanics in sports-related concussions in humans; 9% were not about diagnosis of concussion; 7% were not about sports-related concussions; 5% were not about brain concussions and 1% each were no full papers or reported on less than five players.

We sought to examine 123 full articles. After initial screening, there were 21 disagreements on study inclusion (Cohen's kappa 0.64), and 11 disagreements on the reason for exclusion. These were settled by adjudication and discussion between the two reviewers. After final full-text review, 87 articles were excluded. The most common reason for exclusion was not reporting on clinical criteria of concussion or about biomechanics in sports-related concussions in humans (45%, n=39); other reasons for exclusion were as follows: paper was not about diagnosis of concussion (20%, n=17); was not about brain concussion (16%, n=14); was not about acute effects of concussion (9%, n=8); was not about sports-related concussions (6%, n=5); was no full paper (3%, n=3); or did not require concussion diagnosis being made by medical staff (1%, n=1). Eligible articles represented 2.2% of the total (n=1601) articles.

Supplementary file 2: Risk of bias assessment**QUADAS-2 assessment of included studies**

For included studies reporting original data on the biomechanics of concussion (aim 2), the risk of bias and applicability concerns were assessed using QUADAS-2²⁰ tailored study criteria by one reviewer (AAT). A second reviewer (NFD) confirmed ratings, disagreements were resolved by discussion. Inclusion was not restricted further based upon QUADAS-2 results. We did not apply QUADAS-2 to consensus/statement papers providing definitions of concussion (aim 1).

The QUADAS-2 tool for quality rating of diagnostic accuracy studies consists of four core domains (patient selection, index test, reference standard, and flow and timing).¹ Risk of bias is assessed for all four domains, and applicability is assessed for the first three domains. Thus, seven items per study are assessed to rate quality. For each item the risk of bias is identified as “high”, “low” or “unclear”. QUADAS-2 results are shown in Table 1.

QUADAS-2: risk-of-bias assessment and applicability concerns

Risk of bias and applicability concerns for patient selection were rated as „low“ risk in 16 studies (73%), while in the remaining 6 studies (27%) both items were rated as „high“ risk as only a subset of identified concussions were included in the analysis (see Table 1).

All studies included were considered to have a „high risk“ of bias for index testing as the biomechanical data were analyzed and interpreted with the knowledge of the results from the reference test. As emphasized by Brennan et al.² for a similar review, the validity of biomechanical data recorded could not be adjusted for in this review. We followed the same line of reasoning as Brennan et al.² when assessing applicability concerns for index testing: studies that were either directly funded by or had one/several co-author(s) who had a vested financial interest in the accelerometry system used in each study, were rated as „high risk“. While this was the case in 11 studies (45%), one study was rated as „unclear“ for this item as no information on sources of funding or conflict of interest was provided.³

We considered the risk of bias for the reference standard as „unclear“ in all 22 studies included as it remains unknown whether all concussions were identified by the medical staff or not. As pointed out by Brennan et al.,² however, it is unlikely that all concussions were identified due to the nature of concussions and this cannot be adjusted for in this review. Applicability concerns and flow & timing were considered „low risk“ in all studies included.

Table 1: QUADAS-2 quality ratings for included studies (n=22)

Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow & Timing	Patient Selection	Index Test	Reference Standard
Beckwidth et al. 2009 ⁴	low	high	unclear	low	low	high	low
Beckwidth et al. 2013 ⁵	low	high	unclear	low	low	high	low
Beckwidth et al. 2013 ⁶	low	high	unclear	low	low	high	low
Broglio et al. 2010 ⁷	low	high	unclear	low	low	low	low
Broglio et al. 2011 ⁸	low	high	unclear	low	low	low	low
Brolinson et al. 2006 ⁹	low	high	unclear	low	low	high	low
Duhaime et al. 2012 ¹⁰	high	high	unclear	low	high	high	low
Duma et al. 2005 ¹¹	low	high	unclear	low	low	high	low
Duma and Rowson 2009 ¹²	low	high	unclear	low	low	low	low
Frechede and McIntosh 2009 ¹³	high	high	unclear	low	high	low	low
Funk et 2012 ¹⁴	low	high	unclear	low	low	low	low
Greenwald et al. 2008	low	high	unclear	low	low	high	low
Guskiewics et al. 2007 ¹⁵	low	high	unclear	low	low	low	low
Hernandez et al. 2015 ¹⁶	low	high	unclear	low	low	low	low
King et al. 2015 ¹⁷	low	high	unclear	low	low	low	low
McAllister et al. 2012 ¹⁸	low	high	unclear	low	low	high	low
McIntosh et al. 2000 ¹⁹	high	high	unclear	low	high	low	low
McIntosh et al. 2014 ²⁰	high	high	unclear	low	high	low	low
Patton et al. 2013 ²¹	high	high	unclear	low	high	low	low
Rowson et al. 2012 ²²	low	high	unclear	low	low	high	low
Schnebel et al. 2007 ³	low	high	unclear	low	low	unclear	low
Wilcox et al. 2015 ²³	high	high	unclear	low	high	high	low

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