Concussion in Sport

Research Forum September 2024

Priorities for research to better understand the risks, consequences, prevention and treatment of injuries relating to head impacts in collision sports

Executive Summary

Head impacts in sport can lead to varying degrees of concussion and often result in medical problems such as headache, dizziness and confusion that rapidly resolve. However, some affected may have problems causing significant disability, either because of persisting symptoms or because of the effect of multiple head impacts that accumulate over time.

The importance of recognising these injuries during play is now widely understood and their identification and prevention a priority for many sports. However, there are challenges in developing guidelines for head injury / concussion management that can be applied to all sporting levels, especially at the grassroots level where more needs to be done to help educate participants as to the risks and how to mitigate them.

There is significant variability in both the nature of and response to head injury. Accurate diagnosis is critical to establish the underlying causes of concussive symptoms in participants to guide the appropriate treatment. Furthermore, we need to account for the influence of age, sex, ethnicity and genetic factors on how such individuals respond. Alongside this, the relationship between the nature of head impacts, the force this applies to the brain and the short and longterm outcomes need to be better understood. The cumulative effects of repetitive head impacts have the potential to produce long-term brain injury, for example leading to dementia, and while it remains to be firmly established that sports-mediated head injury directly leads to such outcomes it is imperative that more research is undertaken to investigate this link further.

An expert Research Forum has been established by the UK Government to identify how progress can be made to increase our understanding of the risks associated with head impacts in sport and the mechanisms through which concussion / mild traumatic brain injury (TBI) can affect health and wellbeing, how we can promote more accurate and rapid diagnosis when such events occur, and how we might develop new approaches to prevention and treatment. This has led to the identification of a number of priority areas for future research which are listed here. These are not in any order of priority – all are important to pursue.

- Quantifying the incidence of impacts in sport contributing to TBI and long-term neurodegenerative disease burden.
- Understanding the relationship between head injury biomechanics in terms of i) its causation, ii) the detrimental physiological changes that result and iii) clinical presentation.
- Investigating the effect of sports-related concussion / mild TBI in children and adolescents in the context of developmental trajectories and understanding how differences in age affect short- and long-term effects of head impact exposure.
- To develop point of care / 'pitch side' diagnostics to rapidly confirm the association with concussive symptoms and with high sensitivity and specificity.
- To develop and validate biomarkers that have both diagnostic / prognostic clinical value and/or that provide mechanistic insight into the pathophysiology of sports-related concussion / mild TBI.
- Better understanding of the physiological consequences of concussion / mild TBI and the associated injury processes in order to elucidate the mechanisms that could influence psychological or psychiatric outcomes and/or the initiation and/or progression of neurodegenerative pathology.
- The development of treatments and novel technologies to aid recovery / rehabilitation after concussion / mild TBI.
- Understanding the factors within individuals that modify long term outcomes after head impact exposure, including age, sex, ethnicity, cardiopulmonary fitness and genetic risk.
- Assessment of the impact of guidelines and protocols at different levels of individual sports.
- Evaluation of strategies for prevention and assessment of their impact in reducing the number of clinically relevant head impacts in sport.

In order to undertake such research effectively, a number of wider considerations need to be taken into account. These span:

- the accessibility and use of data from multiple sources and improved data linkage to connect NHS records with large research studies.
- the conduct of research according to statistically robust methodology.
- the networking of high-quality research teams and capabilities to support translational research and help develop more effective preventive strategies and interventions.
- a standardised approach to assess people following concussion / mild TBI, whether at the pitch-side, in General Practice or in A&E/trauma settings, and more accurate diagnosis of neurodegenerative disease.
- balancing discussion regarding the impact and risks of concussion in sport with promoting the health benefits of sporting activity.

- connecting research on concussion in sport to longitudinal population cohorts spanning the lifecourse to help establish population-level risks in sports participation.
- promoting connections to large international studies in this space and partnership with industry, the latter to help develop new diagnostic approaches and treatments.
- the engagement of multiple stakeholder groups

 spanning sporting bodies, healthcare, schools and educational services to improve the quality and consistency of underpinning data and the effectiveness of prevention strategies.

The Research Forum hopes that highlighting the critical knowledge gaps and opportunities to progress important research in this area will provide focus for those organisations with an ability to either fund research, implement the outcomes or develop evidence-based policy, and thereby help promote a concerted and coherent effort to address the issue of concussion in sport.

Introduction

The UK Government's action plan on Concussion in Sport was published in December 2021, providing a framework for mitigating the effects and improving the treatment of concussion in sport for the benefit of everyone taking part. The UK Government's work in this area since then has been structured into three main areas: i) research, ii) education (protocols and guidance), and iii) innovation and technology, with working groups established for each. A key milestone of this work has been the publication in April 2023 by the Government and the Sport and Recreation Alliance of the first UK-wide Concussion Guidelines for Grassroots Sport to help players, coaches, parents, schools, National Governing Bodies and sports administrators to identify, manage and prevent the issue.

The Concussion in Sport Research Forum was established in 2022, bringing together key academic experts with experience of traumatic brain injury (TBI), concussion, physiology, biochemistry, emergency medicine, neurology, neuropsychology, neuropsychiatry, neurosurgery and aligned areas of expertise in order to:

- identify the priority research questions for the sporting sector on an ongoing basis;
- liaise with public funding and sports governing bodies to progress funding opportunities for projects seeking to address the identified research priorities;
- encourage academic institutions, foundations, and other organisations to make concussion in sport one of their priorities and to focus their work in this area around the Research Forum's prioritised list of research aims;
- advise and support the Minister for Sport and their officials in taking forward policy objectives around concussion in sport research.

The Forum's main objective has been to identify the priority research questions that need to be addressed in order to help improve the sector's understanding of the risks and health consequences associated with head impact / concussion in sport. The aim is to use these guestions to provide a framework through which robust evidence can be established to underpin the development of proportionate preventive strategies, new approaches to diagnosis, new and effective treatments, and the better management of longerterm health outcomes. In this way it is envisaged that stakeholders in the sector - spanning sports participants, associations and governing bodies, the health professions, the research community and Government departments – can come together to accelerate progress in promoting safer participation in sport.

Background

Head impacts in sport commonly result in medical problems and there is often uncertainty about how to manage them. 679,000 people attended Emergency Departments in England in the 2022/23 financial year¹ with concerns about traumatic brain injury (TBI) from all causes, including sport. The majority have relatively minor injuries exhibiting concussive symptoms such as headache dizziness, visual disturbance and confusion that rapidly resolve. However, a significant minority have persistent problems causing significant disability, either because of persisting symptoms or because of the effect of multiple head impacts that accumulate over time.

Head injuries can result in a wide range of concussion (Figure 1a). These are seen in sports such as rugby (union and league), football (American and soccer), boxing, wrestling, ice hockey, basketball, horse riding, cycling and motorsport. The importance of recognising these injuries during play is now widely understood and their identification and prevention a priority for many sports. However, there are challenges in developing guidelines for head injury / concussion management that optimally reduce risk, guide treatment and can be applied to all sporting levels. Elite sports generally have sophisticated approaches to identifying and managing potential concussion / mild TBI but it is challenging to apply similar approaches in the grassroots game and more research is needed to develop practical approaches to educating participants and preventing and managing head impacts at all levels.

The symptoms of concussion are non-specific, and it is important to accurately diagnose the underlying causes of common concussive symptoms in participants because different causes require different treatments. For example, dizziness is commonly seen after sporting head impacts. This may be due to TBI but more commonly is the result of peripheral vestibular injury affecting balance. Similarly, headache is sometimes the result of severe brain injury such as an intracranial haemorrhage but in a sports context is much more commonly caused by migraine. A key aim is for research to focus on the pathophysiological mechanisms responsible for such post-traumatic problems. This should include diagnosing the type and severity of brain injury where it is present, but also identifying other mechanisms such as psychiatric / psychological alterations and vestibular disturbance (Figure 1a). Future research should avoid focusing narrowly on describing patterns of concussive

symptoms and instead attempt to understand the cause of problems and develop mechanistically targeted treatments.

It is increasingly recognised that people can respond to head impacts very differently, so we need to better understand the influence of age, sex, ethnicity and genetic factors on this response. For example, the stage of brain development in children and the presence of neurodegenerative pathology in older adults might influence outcome after a head injury substantially. As sporting participation is common (and desirable) in young people, given the general health benefits associated with physical activity, it is particularly important for research to guide how best to reduce risk of injury and optimally manage TBI in children and adolescents.

Attempts to prevent and manage sporting head impacts would benefit greatly from an improved understanding of the relationship between the nature of head impacts (biomechanical forces) and their short and long-term effects (Figure 1a). Traumatic injuries are caused by external forces applied to the brain and other organs at the time of a head impact or rapid acceleration / deceleration event. These can produce injuries of a range of severities, which may or may not lead to symptoms at the time of impact (Figure 1b). In the past it has been challenging to measure these biomechanical forces directly, so defining thresholds for dangerous head impacts has not been possible. The advent of new technologies such as instrumented mouth guards allows sporting head impacts to be routinely measured and their clinical effects studied. This provides a new way to measure head impact exposures and could be particularly informative in understanding the cumulative effects of repetitive head impacts that have not necessarily produced symptoms, but nevertheless could produce long-term brain injury.

There are also significant concerns about the longterm consequences of repetitive sports-related head impacts and concussion / mild TBI, which need to be balanced with the health benefits of sporting participation. The long-term cognitive, psychiatric, and functional consequences of TBI are highly variable and challenging to study. The diagnosis of a dementia, including Alzheimer's disease (AD), is made at higher rates after TBI (from any mode of head injury), while molecular pathologies associated

1. https://digital.nhs.uk/data-and-information/publications/statistical/hospital-accident--emergency-activity/2022-23

with neurodegeneration, including tau and amyloid-B $(A\beta)$, can be observed after both single and repetitive TBI. This provides a potential substrate for the later development of dementias including AD and chronic traumatic encephalopathy (CTE), although it remains to be firmly established that sports-mediated head injury directly leads to such outcomes, and no link has been confirmed in grassroots sports. However, uncertainty about how best to diagnose different post-traumatic pathologies limits our ability to assess and minimise neurodegenerative risk. It is unclear how to accurately diagnose the early stages of post-traumatic dementia and what type of injuries are most risky to brain health. Longitudinal studies are needed to assess long-term outcomes robustly and we will need to systematically apply biomarkers (in body fluids and by neuroimaging) that allow relevant post-traumatic pathology to be measured objectively.

New treatments are also needed for sport related concussion / mild TBI and persisting symptoms that result from this. Given the heterogeneity of posttraumatic problems, the successful development and evaluation of these treatments will depend on accurate diagnosis and treatment stratification. This could be improved dramatically by the application of the wide range of biomarkers that are now available, which promise to improve our ability to identify clinically relevant traumatic pathology. For example, there have been rapid advances in the development of highly sensitive blood / salivary biomarkers of brain trauma, inflammation and neurodegeneration that could aid the identification of traumatic brain injury, clarify what type of injury has occurred and assist with prognostication, including return to play decisions. In the past the classification of TBI has been based on clinical features and more recently neuroimaging findings. In the future it is likely that classification will include a more detailed biomarker driven classification of injury mechanism, which should improve diagnostic, prognostic and treatment decisions.

Figure 1: Concussion Summary: Consequences and Spectrum of Severity

Figure 1a: The consequences of head impacts: biomechanical forces that affect the brain and produce a range of injury mechanisms that lead to the post-traumatic symptoms that are experienced by individuals



The impact that leads to a concussion / mild TBI in a sports context may occur to the head or to the body, with the force of the impact transmitting energy and acceleration / deceleration and rotational forces to the head. This can lead to a degree of brain injury (chemical / electrical disturbance to brain cells) and in more severe cases to a contusion injury (bleeding / bruising of brain tissue) or axonal injury (structural injury to the connections of the nerve cells). However, in the vast majority of concussion / mild TBI occurring in a sports context, routine imaging of the brain does not show signs of structural brain injury. Regardless, these head impacts can lead to a range of symptoms indicating a disturbance of brain function.

Figure 1b: Spectrum of traumatic brain injury severity



Severity of TBI: (i) Subclinical TBI: head impact with no associated neurological deficit; (ii) Symptomatic (possible) TBI: head impact producing concussive symptoms only; (iii) Mild Probable TBI: head impact producing short lasting loss of consciousness (< 30 minutes), post-traumatic amnesia (momentary to 24 hours) and or depressed basilar or linear skull fracture (dura intact); (iv) Moderate/Severe TBI: head impact leading to death; loss of consciousness > 30 minutes; post-traumatic amnesia > 24 hours; Glasgow Coma Score < 13/15 in the initial 24 hours; and/or neuroimaging findings of intracerebral, subdural, epidural, or subarachnoid haemorrhages; cerebral or haemorrhagic contusion, penetrating TBI, or brainstem injury.

Note that the severity of TBI here refers to the acute phase, rather than later consequences of injury.

* Relates to Mayo Classification approach [Malec et al (2007) Journal of Neurotrauma Vol. 24, No. 9].

Research Priorities

The Forum has identified how progress can be made to increase our understanding of the risks associated with concussion in sport and the pathophysiology of concussion / mild TBI, how we can promote more accurate and rapid diagnosis, and how to develop new approaches to prevention and treatment. Accordingly, ten areas have been identified that are considered priorities for future research. Some represent areas of incomplete understanding, while others address fundamental knowledge gaps. These areas are listed below and are not presented in order of priority – all are important to progress.

Underpinning all is the need to recognise that concussion/TBI collectively constitutes a syndrome (see Figure 1b), where current heterogeneity complicates both research, diagnosis and intervention. For the purposes of this paper the term concussion / TBI is used to cover all aspects of head trauma, and for future studies it will be important to specify where subject selection and analysis falls on this spectrum.

Quantifying the incidence of impacts in sport contributing to concussion / mild TBI and long-term neurodegenerative disease burden.

There is accumulating evidence that a career in contact sports is associated with an increased risk of neurodegenerative disorders including dementia. More knowledge on the unbiased risks and benefits of sports participation is required. Research with a particular focus on short-term and long-term brain health is needed, with increased consideration of the shifting demographics in many sports (e.g. the increasing popularity of new disciplines and female participation in contact sport). There is already much available data that needs linkage and correlation between health records, injury registries and sports medicine participant data in large studies at population level. More severe traumatic brain injuries should not be included, though it is recognised these can be a rare consequence of head impact in sport. New and improved registries - potentially with a focus on atrisk, high-participation sports such as rugby, soccer and other contact sports - should be established and stratified by type of sport, age, sex and ethnicity.

Studies should also correlate sporting activity to injury-related outcomes at elite and grassroots level, while the concussed athletes should be followed across the lifespan in the context of associated longevity and quality of life. Research should consider concussion / mild TBI injuries alongside longer-term neurodegenerative outcomes and engage with sporting participants throughout the research but particularly when framing findings for dissemination.

Understanding the relationship between head injury biomechanics in terms of i) aetiology, ii) pathophysiology and iii) clinical presentation.

Relatively little is known about the forces that can impact the head in different sports and how these relate to concussion / mild TBI and longer-term risks of brain injury. Aetiological considerations include the type and level of sport (e.g. training versus match play; elite and grassroot levels), and how risks relate to individual severe impacts and the combined effects of more minor impacts. The causes of concussion / mild TBI also differ between sexes, ages and with the social context. To assess pathophysiology, there is a need to consider head / body impact, linear / rotational forces, thresholds for increased risk from single and cumulative impacts and the relationship of biomechanics to metabolic and neuroimaging findings. Clinical presentation refers to acute-, mid- and longer-term physical, neuropsychological, neuropsychiatric and neurodegenerative outcomes. Research should support the development and use of technology, including wearables, to better define the potential relationships between biomechanical impacts, symptoms, outcomes and interventions / countermeasures.

Investigating the effect of sports-related concussion / mild TBI in children and adolescents in the context of developmental trajectories and understanding how differences in age affect short- and long-term effects of head impact exposure.

Participation in sport benefits children's physical and mental health, with highly positive effects that carry forward into adult life. The risks – and therefore appropriate mitigations – of concussion / mild TBI are likely to vary by age, sex and other demographic factors, and by sport, which needs to be better understood. Research should examine the mechanisms that influence these risks in children and young people, including the effects of anatomical differences (e.g. in skull and musculature), health, education and socioeconomic status, sports preferences, and early medical and educational interventions. Knowledge gaps include understanding how concussion / mild TBI affects developmental trajectories and how these events relate to the risk of adult neurological, psychiatric and co-morbid consequences. An assessment of the net benefits and risks of different activities is needed alongside research into effective messaging to retain and promote the positive benefits of sport, which may vary by sport, age, ethnicity, and socioeconomic settings. Prevention strategies are required for sport-related concussion / mild TBI in young people using evidencebased approaches and stakeholder inclusion.

To develop point of care / 'pitch side' diagnostics to confirm the association with concussive symptoms rapidly with high sensitivity and specificity.

Current diagnosis of sports-related concussion / mild TBI relies solely on athlete symptoms and clinical signs that are infrequent, non-specific and open to subjective interpretation, and in the context of elite sports on pitch-side assessments which have only limited sensitivity and specificity. There is an urgent need for more scalable and robust biomarkers to provide a more objective, timely and personalised diagnosis of mild TBI across all ages and competencies to better inform return-to-play protocols and long-term healthcare assessment. Since concussion / mild TBI initiates transient disturbance of central nervous system function, techniques used to measure impaired brain structure and function, or other evidence of brain injury, could aid in diagnosis. Ideally, the diagnosis should occur rapidly at 'pitch-side'. Such techniques include molecular biomarker signatures that can be detected in blood, saliva or urine using user-friendly sampling methods and portable analysis devices for immediate analysis (point-of-care). In addition, assessment of cognitive function, tracking of eye movement, analysis of the electrophysiological activity of the brain and recent advances in portable, ultra-lowfield magnetic resonance brain imaging all lie in scope. Inertial sensor technology that includes instrumented helmets, headbands, skin patches, mouthquards and earplugs can help define the relationship between biomechanical impacts and concussion / mild TBI.

To develop and validate biomarkers that have both diagnostic / prognostic clinical value and/ or that provide mechanistic insight into the pathophysiology of sports related concussion / mild TBI.

The development of biomarkers has the potential to advance the identification and management of sportsrelated concussion / mild TBI significantly. Potential biomarkers include those derived from neuroimaging, such as magnetic resonance imaging, positron emission tomography and magnetoencephalography.

These could be used to characterise functional and structural effects of head trauma on the brain, both immediately and in the longer-term, including changes in cerebral metabolism, inflammation and brain network functioning. In addition, biomarkers measured in blood or other fluids may allow the presence and severity of a range of pathologies to be measured. When coupled with biomechanical description of head impact severity, the measurement of biomarkers may allow injury thresholds to be defined. This could help to establish which kinds of head impacts increase the risk of TBI, cognitive impairment and later neurodegeneration. Biomarkers also have the potential to inform the development and evaluation of new interventions aimed at improving outcomes after sporting injury or reducing the risk of harm caused by head impacts in sport, even during games (for example in elite sport).

Better understanding of the pathophysiology of concussion / mild TBI and the associated injury processes in order to elucidate the mechanisms that could influence psychological or psychiatric outcomes and/or the initiation and/or progression of neurodegenerative pathology.

Animal models provide insights into the extent to which mechanically induced mild traumatic brain injury impacts molecular, haemodynamic and structural components of the central nervous system adversely. However, there is an urgent need for translational research to better understand the initiation and progression of human brain injury from sports related concussion. This encompasses acute injury mechanisms, aberrant behavioural responses and delayed or secondary neurodegenerative pathologies. Translational models need to accommodate the interactions with age (including development, adolescence, mid-life progression and later-life degeneration), sex, sport type and level, genetics and behaviours, including medication usage. An integrative, multidisciplinary approach is required to understand the complex pathophysiology of sports related concussion / mild TBI, informed by personalised, multimodal molecular-neuroimaging biomarkers.

This work should be directed towards (i) phenotyping of injury biomechanics and acute secondary mechanisms of cell damage (ii) corresponding relationships to acute symptomatology and behavioural response and (iii) factors that promote or protect from development of long-term neurological, neuropsychological and neuropsychiatric outcomes. Large-scale, unbiased, autopsy studies are also warranted to quantify the burden of neurodegeneration, building on closer international linkage and collaboration.

The development of treatments and novel technologies to aid recovery / rehabilitation after concussion / mild TBI.

There is a need to develop new treatments (pharmacological, neuromodulatory, psychotherapeutic and rehabilitative), coupled to the development of novel technologies, for perisisting symptoms and/or specific symptom clusters (e.g. vestibular, migraine, anxiety, hypersensitivity, cognitive complaints, etc.) to aid recovery / rehabilitation after concussion / mild TBI. Developing the incorporation of biomarkers into both patient selection and outcomes is required to enrich evaluation of early-stage clinical studies. Alongside this, there is a need for validation and implementation science to assess and optimize the use of novel technologies in both clinical and real-world settings. Helping to define the optimum time window and duration of treatments is also needed to mitigate longer-term effects of concussion and to evaluate the potential of such interventions themselves to cause inadvertent harm.

Understanding the factors within individuals that modify long term outcomes after head impact exposure, including age, sex, ethnicity, cardiopulmonary fitness and genetic risk.

Sports related concussion / mild TBI leads to a wide range of long-term outcomes, with a high cumulative burden in physical and mental health, social and economic costs. However, there is wide variation in these outcomes, which is only partly explained by the biomechanics of the injury itself. The identification of outcome modifiers can reveal mechanisms of long-term harm, raising new therapeutic strategies for secondary prevention. Recognised modifiers of outcome also enable the stratification for interventions, targeting those at higher long-term risk and balancing the risks and benefits of continuing sports participation. Potential modifiers of outcome include (i) early interventions, based on awareness, education and initial medical, behavioural or lifestyle intervention after injury; (ii) lifespan context, including education, ethnicity, developmental stage and age, adversity and family or peer support networks; (iii) co-morbid physical and mental health conditions, including fitness; (iv) genetic moderators of resilience, repair and recovery. Research priorities include enduring effects after injury (e.g. persisting psychiatric, cognitive or educational problems) or delayed consequences (e.g. late neurodegeneration).

Assessment of the impact of guidelines and protocols at different levels of individual sports.

In recent years there has been much work put into developing guidelines and protocols for the evaluation and management of concussion / mild TBI in sport. There is limited knowledge on how these guidelines and protocols are implemented, to what extent they are adhered to at different sports levels and how they have changed the behaviour of or outcomes for the athlete. Research should also explore athlete's awareness and attitudes towards risk of concussion and potential longer term health impacts in sports. Where possible, studies should differentiate how guideline and protocol adherence varies according to age, sex, ethnicity, type and level of sport participation, as well as to socioeconomic status. Research should be targeted and stratified to identify how adherence to guidelines / protocols influences symptom duration and long-term outcome. Findings should be framed in partnership with sporting communities in order to refine current management of the concussed athlete and improve understanding of the social and behavioural consequences of concussion / mild TBI in sport at a population level.

To evaluate strategies for prevention and assess their impact in reducing the number of clinically relevant head impacts in sport.

Research is needed to assess the effectiveness of strategies preventing sport-related acute traumatic brain injury and the potential development of later neurodegenerative diseases. The research should consider impacts that lead to objective evidence of TBI and repetitive subclinical TBI that can still have long-term consequences. Strategies being evaluated could be Primary (general or targeted – according to cumulative risk - prevention of head impacts during sport); Secondary (reducing the likelihood of brain injury after any head impact) and Tertiary (clinical management to improve post impact outcomes). These could be considered in isolation or in combination as per the conceptualisation of Haddon's Matrix, a tool used in the field to combine host and environmental considerations with these different phases of injury. Research needs to establish the clinical and cost effectiveness of preventive strategies and the acceptability of interventions to sport participants across the lifespan at grassroots and elite level.

Research Enablers and Wider Considerations

There are a number of wider considerations that need to be taken into account in pursuing the above research agenda to best effect:

- The amount of data which will be generated through epidemiology, biomarker research and technological advances in monitoring and assessing concussion / mild TBI in sport will require a data framework to be developed. This should address the need to adopt 'big data' standards, such as the FAIR guidelines, the identification of common data elements to promote data integration, interoperability and systematic data sharing and the promotion of wide accessibility and analysis. Of particular note in this regard is the recent establishment of TBI-REPORTER (a national research platform funded by MRC/UKRI, Department of Health and Social Care, Ministry of Defence and Alzheimer's Research UK) which will provide a national data hub and biomarker resource for TBI-related research.
- All research needs to utilise statistically robust methodology and ensure that confounding factors are accounted for in assessing long-term outcome, and that appropriate statistical power is provided to adequately detect any given treatment effect. Effort will be needed to 'network' those close to the sporting activity with the research community to ensure appropriate application of the best research practice.
- Understanding the biological and pathophysiological mechanisms that underlie ill health following concussion / mild TBI will benefit from pre-clinical research and linkages to established centres of excellence in brain health and neurophysiology.
 Better experimental models to study TBI are being developed by a number of labs and linkage to clinical research will provide the opportunity for bidirectional translational research with a view to developing more effective interventions.
- On the clinical side, a standardised approach is needed to assess people following concussion / mild TBI, whether at the pitch-side, in General Practice or in Accident & Emergency / trauma settings, as well as those presenting late to services. A more standardised framework for TBI biomarkers

would be helpful in this respect. Coupled to this, diagnosis of neurodegenerative disease post TBI needs to be more precise and standardised to avoid errors in diagnosis and unnecessary patient anxiety. An opportunity here is the recently created UK Concussion Network (UKCN), through which over 20 centres across the UK have been linked to provide access to treatment and care after concussive events. The UKCN offers the prospect of a research enabled clinical network and the provision of standardised routes to diagnosis and assessment.

- The messaging of the impact and risks of concussion in sport needs to be carefully managed as practising sport is beneficial to health and wellbeing, with an appropriate balance needed to promote sporting activity but more safely. This will need consideration with respect to demographic aspects such as age, sex and socio-economic background.
- Embedding suitable surveys and/or measures in longitudinal population cohorts spanning the lifecourse would provide valuable prospective data in support of the concussion in sport research agenda and to better understand the risks / benefits of sport participation. Opportunities should be explored to influence ongoing large population studies regarding data collection in order to provide an effective way of establishing population risks in sports participation, for example the new MRC/UKRI-funded Adolescent Health Study which will establish a long-term prospective study to look at developmental influences affecting health and well-being through childhood and adolescence. Opportunities may also exist through long-established cohorts which combine biomedical and lifestyle data at scale across other age-ranges, such ALSPAC, UK Biobank, Our Future Health etc.
- Rigorous epidemiological research will depend on new approaches to data collection and sharing as well as improved data linkage to connect sportspecific data and NHS records with large research studies. A particular challenge will be collecting data on the ground in both elite and community sport, where the frameworks for doing so are somewhat limited.

- Opportunities should be explored to establish linkage with other large international studies in this space – for example, the <u>NCAA- DoD Grand</u> <u>Alliance-funded Care Consortium</u> in the USA, the <u>International Initiative for TBI research (InTBIR)</u> and the <u>European Neurotrauma Organisation</u> – as well as the datasets held by other overseas sport governing bodies such as the NFL in the USA. In combination with the aforementioned data framework, this would widen the scope for federated or conventional analyses of multiple large datasets.
- Progress in developing new diagnostic approaches and treatments requires partnership with industry (spanning the life sciences, technological and digital) and approaches for networking relevant interest groups should be considered. The need to integrate end-user (i.e. sport participants) perspectives in this dialogue at an early stage is essential.
- The quality and consistency of data, and the effectiveness of primary and secondary prevention strategies, will depend on multiple stakeholder engagement. Stakeholders include the governing bodies of major sports, and grassroots networks, which vary in format and coverage between sports. Primary and secondary health care sectors are likely to need different modes of engagement, beyond services directly providing care to people with TBI, with training, referral and treatment pathways all made accessible. Schools and educational psychology services, and social services supporting children and adolescents play a critical role in awareness, training, recognition of acute and delayed effects of concussion / mild TBI and longterm support for those affected. The quality and impact of research and interventions will benefit from cross-sector stakeholder engagement in design as well as the execution of research.

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References

Abrahams, S., Fie, S.M., Patricios, J., Posthumus, M., and September, A.V. (2013) 'Risk factors for sports concussion: an evidence-based systematic review', British Journal of Sports Medicine, 48(2), pp.91–97. DOI: <u>https://doi.org/10.1136/bjsports-2013-092734</u>.

Covassin, T., Savage, J.L., Bretzin, A.C., and Fox, M.E. (2018) 'Sex differences in sport-related concussion long-term outcomes', International Journal of Psychophysiology, 132, pp.9–13. DOI: 10.1016/j.ijpsycho.2017.09.010.

Craig, D.I., Lininger, M.R., Vomacka, M.M., and Tiscareno, R. (2019) 'Concussion reporting behaviors of athletes: A systematic review', Athletic Training & Sports Health Care, 12(2), pp.81–88. DOI: 10.3928/19425864-20190322-01.

Echemendia, R.J., Brett, B.L., Broglio, S.P., Davis, G.A., Giza, C.C., Guskiewicz, K.M., Harmon, K.G., Herring, S., Howell, D.R., Master, C., McCrea, M., Naidu, D., Patricios, J., Putukian, M., Walton, S.R., Schneider, K.J., Burma, J.S., and Bruce, J.M. (2023) 'Sport concussion assessment tool[™] – 6 (SCAT6)', British Journal of Sports Medicine, 57(11), pp.622–631. Available at: https://doi.org/10.1136/bjsports-2023-107036.

Eckner, J.T., Kutcher, J.S., Broglio, S.P., and Richardson, J.K. (2014) 'Effect of sport-related concussion on clinically measured simple reaction time', British Journal of Sports Medicine, 48(2), pp.112–118. DOI: 10.1136/ bjsports-2012-091579.

Eliason, P.H., Galarneau, J.-M., Kolstad, A.T., Pankow, M.P., West, S.W., Bailey, S., Miutz, L., Black, A.M., Broglio, S.P., Davis, G.A., Hagel, B.E., Smirl, J.D., Stokes, K.A., Takagi, M., Tucker, R., Webborn, N., Zemek, R., Hayden, A., Schneider, K.J., and Emery, C.A. (2023) 'Prevention strategies and modifiable risk factors for sport-related concussions and head impacts: a systematic review and meta-analysis', British Journal of Sports Medicine, 57(12), pp.749–761. DOI: 10.1136/bjsports-2022-106656.

Guskiewicz, K.M., McCrea, M., Marshall, S.W., Cantu, R.C., Randolph, C., Barr, W., Onate, J.A., and Kelly, J.P. (2003) 'Cumulative effects associated with recurrent concussion in collegiate football players', The Journal of the American Medical Association, 290(19), pp.2549-2555. DOI: 10.1001/jama.290.19.2549.

Helmy A., Agarwal M., Hutchinson P.J. (2013) 'Concussion and sport' BMJ, Sep 25:347:f5748. doi: 10.1136/bmj.f5748.

Holmes, A., Chen, Z., Yahng, L., Fletcher, D., and Kawata, K. (2020) 'Return to learn: Academic effects of concussion in high school and college student-athletes', Frontiers in Pediatrics, 8, pp.57. DOI: 10.3389/ fped.2020.00057.

Kirk, B., Pugh, J., Cousins, R. and Phillips, S. (2018) 'Concussion in university level sport: Knowledge and awareness of athletes and coaches', Sports, 6(4), p.102. DOI: 10.3390/sports6040102.

Leddy, J.J., Burma, J.S., Toomey, C.M., Hayden, A., Davis, G.A., Babl, F.E., Gagnon, I., Giza, C.C., Kurowski, B.G., Silverberg, N.D., Willer, B., Ronksley, P.E., and Schneider, K.J. (2023) 'Rest and exercise early after sport-related concussion: A systematic review and meta-analysis', British Journal of Sports Medicine, 57(12), pp.762–770. DOI: 10.1136/bjsports-2022-106676.

Lumba-Brown, A., Teramoto, M., Zhang, R., Aukerman, D.F., Bohr, A.D., Harmon, K., Petron, D.J., Romano, R., Poddar, S.K., and Ghajar, J. (2023) 'Multicentre evaluation of anxiety and mood among collegiate student athletes with concussion', BMJ Open Sport & Exercise Medicine, 9(1), p.e001446. DOI: 10.1136/bmjsem-2022-001446.

Manley, G., Gardner, A.J., Schneider, K.J., Guskiewicz, K.M., Bailes, J., Cantu, R.C., Castellani, R.J., Turner, M., Jordan, B.D., Randolph, C., Dvořák, J., Hayden, K.A., Tator, C.H., McCrory, P., and Iverson, G.L. (2017) 'A systematic review of potential long-term effects of sport-related concussion', British Journal of Sports Medicine, 51(12), pp.969-977. DOI: 10.1136/bjsports-2017-097791.

Master, C.L., Katz, B.P., Arbogast, K.B., McCrea, M.A., McAllister, T.W., Pasquina, P.F., Lapradd, M., Zhou, W., and Broglio, S.P. (2020) 'Differences in sport-related concussion for female and male athletes in comparable collegiate sports: A study from the NCAA-DoD Concussion Assessment, Research and Education (CARE) Consortium', British Journal of Sports Medicine, pp.1387-1394. DOI: 10.1136/bjsports-2020-103316.

McCrory, P., Meeuwisse, W.H., Aubry, M., Cantu, B., Dvořák, J., Echemendia, R.J., Engebretsen, L., Johnston, K., Kutcher, J.S., Raftery, M., Sills, A., Benson, B.W., Davis, G.A., Ellenbogen, R.G., Guskiewicz, K., Herring, S.A., Iverson, G.L., Jordan, B.D., Kissick, J., and McCrea, M. (2013) 'Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012', British Journal of Sports Medicine, 47(5), pp.250–258. DOI: 10.1136/bjsports-2013-092313.

McKee, A.C., Cantu, R.C., Nowinski, C.J., Hedley-Whyte, E.T., Gavett, B.E., Budson, A.E., Santini, V.E., Lee, H.-S., Kubilus, C.A., and Stern, R.A. (2009) 'Chronic traumatic encephalopathy in athletes: Progressive tauopathy after repetitive head injury', Journal of Neuropathology & Experimental Neurology, 68(7), pp.709–735. DOI: 10.1097/ NEN.0b013e3181a9d503.

Montenigro, P.H., Alosco, M.L., Martin, B.M., Daneshvar, D.H., Mez, J., Chaisson, C.E., Nowinski, C.J., Au, R., McKee, A.C., Cantu, R.C., McClean, M.D., Stern, R.A., and Tripodis, Y. (2017) 'Cumulative head impact exposure predicts later-life depression, apathy, executive dysfunction, and cognitive impairment in former high school and college football players', Journal of Neurotrauma, 34(2), pp.328–340. DOI: 10.1089/neu.2016.4413

Patricios, J.S., Schneider, K.J., Dvorak, J., Ahmed, O.H., Blauwet, C., Cantu, R.C., Davis, G.A., Echemendia, R.J., Makdissi, M., McNamee, M., Broglio, S., Emery, C.A., Feddermann-Demont, N., Fuller, G.W., Giza, C.C., Guskiewicz, K.M., Hainline, B., Iverson, G.L., Kutcher, J.S., and Leddy, J.J. (2023) 'Consensus statement on concussion in sport: the 6th International Conference on Concussion in Sport–Amsterdam, October 2022', British Journal of Sports Medicine, 57(11), pp.695–711. DOI: 10.1136/bjsports-2023-106898.

Pei, Y., Kemp, A.M., and O'Brien, K.H. (2023) 'Investigating the student in returning to learn after concussion: A systematic review and meta-analysis', Journal of School Health, 93, pp.594-620. DOI: 10.1111/josh.13307.

Publications Parliament UK (2021). Concussion in sport - Digital, Culture, Media and Sport Committee - House of Commons. Available at: https://publications.parliament.uk/pa/cm5802/cmselect/cmcumeds/46/4602.htm.

Putukian, M., Purcell, L., Schneider, K.J., Black, A.M., Burma, J.S., Chandran, A., Boltz, A., Master, C.L., Register-Mihalik, J.K., Anderson, V., Davis, G.A., Frémont, P., Leddy, J.J., Maddocks, D., Zahra Premji, Ronksley, P.E., Herring, S., and Broglio, S.P. (2023) 'Clinical recovery from concussion–return to school and sport: a systematic review and meta-analysis', British Journal of Sports Medicine, 57(12), pp.798–809. DOI: 10.1136/bjsports-2022-106682.

Rashid, H., Mishra, S., and Dobbin, N. (2021) 'Management of sport-related concussion in emergency departments in England: A multi-center study', Brain Injury, 35(9), pp.1035–1042. DOI: 10.1080/02699052.2021.1945146.

Rice, S.M., Parker, A.G., Rosenbaum, S., Bailey, A., Mawren, D., and Purcell, R. (2017) 'Sport-related concussion and mental health outcomes in elite athletes: A systematic review', Sports Medicine, 48(2), pp.447–465. DOI: 10.1007/s40279-017-0810-3.

Rigney, G.H., Jo, J., Burns, C., Williams, K.L., Terry, D.P., and Zuckerman, S.L. (2023) 'Do academic accommodations help students recover following sport-related concussion? A retrospective study of 96 youth athletes', Journal of Neurosurgery: Pediatrics, 33(2), pp.109–117. DOI: 10.3171/2023.9.PEDS23241.

Scullion, E., and Heron, N. (2022) 'A scoping review of concussion guidelines in amateur sports in the United Kingdom', International Journal of Environmental Research and Public Health, 19(3), p.1072. DOI: 10.3390/ijerph19031072.

Seifert, T.D. (2013) 'Sports concussion and associated post-traumatic headache', Headache: The Journal of Head and Face Pain, 53(5), pp.726–736. DOI: 10.1111/head.12087.

Stewart,W., Buckland, M.E., Abdolmohammadi, B., Affleck, A. J., Alvarez, V. E., Gilchrist, S., Huber, B.R., Lee, E.B., Lyall, D.M., Nowinski, C.J., Russell, E.R., Stein, D.T., Suter, C.M., and McKee, A.C. (2023) 'Risk of chronic traumatic encephalopathy in rugby union is associated with length of playing career', Acta Neuropathol., 146(6), pp. 829–832. DOI: 10.1007/s00401-023-02644-3

Tator, C.H. (2013) 'Concussions and their consequences: current diagnosis, management and prevention', Canadian Medical Association Journal, 185(11), pp.975–979. DOI: 10.1503/cmaj.120039.

Tator, C.H. (2012) 'Sport concussion education and prevention', Journal of Clinical Sport Psychology, 6(3), pp.293–301. DOI: 10.1123/jcsp.6.3.293.

UK Government (2023). Landmark concussion guidance for grassroots sport published. Available at: https://www.gov.uk/government/news/landmark-concussion-guidance-for-grassroots-sport-published#:~:text=.

Walshe, A., Daly, E., and Ryan, L. (2022) 'Epidemiology of sport-related concussion rates in female contact/ collision sport: A systematic review', BMJ Open Sport & Exercise Medicine, 8(3), p.e001346. DOI: 10.1136/ bmjsem-2022-001346.

Yeo, P.C., Yeo, E.Q.Y., Probert, J., Sim, S.H.S., and Sirisena, D. (2020) 'A systematic review and qualitative analysis of concussion knowledge amongst sports coaches and match officials', Journal of Sports Science & Medicine, 19(1), pp.65–77. PMCID: PMC7039019.

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