Original research

Sports-related concussion not associated with long-term cognitive or behavioural deficits: the PROTECT-TBI study

Matthew Joseph Lennon [1,2] Grant Rigney,[3] Byron Creese,[4,5] Dag Aarsland,[6,7] Adam Hampshire,[8] Clive Ballard,[5] Anne Corbett,[5] Vanessa Raymont[2]

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[1]Faculty of Medicine and Health, University of New South Wales, Sydney, New South Wales, Australia
[2]Department of Psychiatry, University of Oxford, Oxford, UK
[3]Harvard Medical School, Harvard University, Cambridge, Massachusetts, USA
[4]Division of Psychology, Department of Life Sciences, Brunel University London, Uxbridge, UK
[5]Department of Health and Community Sciences, College of Medicine and Health, University of Exeter, Exeter, UK
[6]Department of Old age Psychiatry, IoPPN, King's College London, London, UK
[7]Centre for Age-related research, Stavanger University Hospital, Stavanger, Norway
[8]Department of Brain Sciences, Faculty of Medicine, Imperial College London, London, UK

Correspondence to
Dr Vanessa Raymont; Vanessa.raymont@psych.ox.ac.uk

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ABSTRACT

Background The cognitive effects of sports-related concussion (SRC) have been the subject of vigorous debate but there has been little research into long-term outcomes in non-athlete populations.

Methods This cohort study of UK community-dwelling adults (aged 50–90 years) was conducted between November 2015 and November 2020, with up to 4 years annual follow-up (n=15 214). Lifetime history of concussions was collected at baseline using the Brain Injury Screening Questionnaire. The first analysis grouped participants by type of concussion (no concussion, only SRC, only non-SRC (nSRC), mixed concussions (both SRC and nSRC)) and the second grouped the participants by number (0, 1, 2 or 3+ SRC or nSRC). Mixed models were used to assess the effect of concussion on outcomes including four cognitive domains and one behavioural measure (Mild Behavioural Impairment-C).

Results Analysis of the included participants (24% male, mean age=64) at baseline found that the SRC group had significantly better working memory (B=0.113, 95% CI 0.038, 0.188) and verbal reasoning (B=0.199, 95% CI 0.092, 0.306) compared with those without concussion. Those who had suffered one SRC had significantly better verbal reasoning (B=0.111, 95% CI 0.031, 0.19) and attention (B=0.115, 95% CI 0.028, 0.203) compared with those with no SRC at baseline. Those with 3+ nSRCs had significantly worse processing speed (B=–0.082, 95% CI –0.144 to –0.019) and attention (B=–0.156, 95% CI –0.248 to –0.063). Those with 3+ nSRCs had a significantly worse trajectory of verbal reasoning with increasing age (B=–0.088, 95% CI –0.149 to –0.026).

Conclusions Compared with those reporting no previous concussions, those with SRC had no cognitive or behavioural deficits and seemed to perform better in some tasks. As indicated by previous studies, sports participation may confer long-term cognitive benefits.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Recurrent sports-related concussion (SRC) in professional athletes is associated with significantly greater risk of mild cognitive impairment (MCI) and dementia, but long-term cognitive outcomes after SRC in non-professional athletes are not known.

WHAT THIS STUDY ADDS

⇒ This UK-based community-based longitudinal cohort study (n=15 214, age range=50–90 years) showed that those with SRC showed no long-term cognitive or behavioural deficits compared with those with no concussions.
⇒ In fact, they showed better performance in working memory and verbal reasoning at the study baseline.
⇒ By contrast, those with non-SRC showed deficits in processing speed, attention and the Mild Behavioural Impairment (MBI-Checklist) index.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study suggests that the cognitive risks of concussion in sport may not be meaningful in the long term in the non-professional athlete population.
⇒ These results will help inform physicians and public health authorities when communicating the risks and benefits of community sports to patients and the public.

INTRODUCTION

Approximately 2% of the UK population present to emergency annually with a head injury[1] and it is the leading cause of death in those under 40 years of age. Traumatic brain injury (TBI) can increase dementia risk by 1.5–3 times and estimates indicate that TBI contributes 5–15% of the current dementia burden.[2]

TBIs vary in classification from 'mild' (a temporary change in mental status or loss of consciousness (LOC) of less than 30 min) to 'moderate-severe' (prolonged amnesia or LOC more than 30 min).[3] The most frequent causes of mild TBI are assaults, falls and road traffic collisions,[1] but among children and adolescents, sports-related mild TBI is the second most common cause, affecting 0.3–0.4% of adolescents annually.[4] This type of mild TBI is most commonly referred to as sports-related concussion (SRC) in the literature. The impact of SRC on long-term cognitive outcomes and dementia has been the subject vigorous public debate, having been highlighted by many high-profile cases of professional athletes.

Among athletes, there seems to be a relationship between repeated SRC and poor cognitive outcomes. In a meta-analysis including 21 studies of athletes (n=790 concussion cases, 2014 controls), ranging from high school to professional, there were substantial deficits in the first few days of injury that all essentially resolved by 7–10 days of recovery.[5] In a more recent meta-analysis of 11 studies (n=792), Zhang *et al*[6] compared retired elite athletes who had suffered SRC years earlier with those who had not suffered concussion. The concussed group demonstrated mild to moderate deficits in verbal memory (Standardized Mean Difference (SMD)=−0.29), delayed recall (SMD=−0.30) and attention (SMD=−0.33). In their seminal study of mid-life retired American football players (n=2552), Guskiewicz *et al*[7] found that those with recurrent concussion had five times the rate of clinically diagnosed MCI and three times the rate of subjective memory impairment compared with non-concussed retired players. Based on these data, advocates argue that recreational contact sport, particularly in young people, is too risky and should be discouraged or banned. Yet, there is very little research on long-term outcomes of SRC in the non-collegiate or professional athlete population. Professional athletes are disproportionately male[8] and comprise only a tiny fraction of the population. They are exposed to a considerably greater number, frequency and severity of concussions, as well as more repetitive subconcussive head impacts compared with the non-athlete population.[5] Given the ubiquity of concussions in community sport, it is critical that the long-term cognitive outcomes of these injuries are understood in a community-dwelling population rather than just in professional athletes.

The extant research focuses largely on cognitive outcomes rather than behavioural changes. Mild behavioural impairment (MBI) is a well-established description[9] of late-life onset, sustained behavioural and personality changes that are associated with biomarkers of neurodegenerative disease, worsening cognitive impairment and dementia.[9] One recent study by Bray *et al*[10] examined 124 participants with a self-reported history of concussion, as they progressed from normal cognition to a dementia diagnosis. They found that concussion was significantly associated with a dementia prodrome of greater social inappropriateness compared with controls. Thus, MBI may be a useful adjunct to cognitive measures in a comprehensive assessment of concussion-induced deficits.

This study examines the associations between SRC, non-sports-related concussion (nSRC) (ie, concussions in contexts other than active sports) and long-term cognitive and behavioural outcomes in a longitudinal cohort of community-dwelling adults. Specifically, it examines whether there are different profiles of cognitive and behavioural deficits for SRC and nSRCs.

METHODS

Participant population

The PROTECT study (www.protectstudy.org.uk) is a UK-based longitudinal study of 50–90 year olds.[11] For eligibility, participants were required to have access to a computer and all those with previously diagnosed dementia at baseline were excluded. All participants gave informed consent prior to involvement and were assessed at baseline (wave 1) and then had up to 4 years of annual assessments (waves 2–5) between November 2015 and November 2020. A full description of the study can be found in prior publications.[11] This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline (online supplemental table S1).

Classification of concussion

The Brain Injury Screening Questionnaire (BISQ)[12] was used to collect data on previous concussions/TBIs. It was an optional, self-administered battery within the PROTECT study, and of eligible participants with sufficient data in the PROTECT study, 4379 individuals did not complete the BISQ and 15 764 did. The baseline characteristics of responders and non-responders are compared in online supplemental table S2 to assess for self-selection bias. This questionnaire collects data on lifetime history of head injuries asking specifically, 'Have you ever had a blow to the head … [in a particular context for example, on a motorcycle/all-terrain vehicle]'. Participants are asked about the context of the injury (sports related, motor vehicle crash, etc), the age of the first/last TBI, the severity of each episode (length of time unconscious/dazed or confused) and the number of injuries.

Similar to a previous publication from this cohort,[13] head injuries were classified using the Mayo TBI Severity Classification System.[3] Concussion (mild or symptomatic TBI) was defined as a head injury followed by LOC of less than 30 min or a dazed or confused episode. Moderate-severe TBI was defined as a head injury followed by a LOC of 30 min or longer. Each concussion was classified as either sports related (occurring while biking or playing sports)[14] or non-sports related (occurring from another cause) (nSRC). For the head injury questions comprising the BISQ, see online supplemental table S3. As there were only a small number of moderate-severe TBI acquired during sports, it was not possible to analyse them separately, and thus for all analyses, any participants with moderate-severe TBI were removed (total moderate-severe TBI n=510, sports-related moderate-severe TBI n=53), only assessing those with concussion (mild or symptomatic TBI). Online supplemental table S4 compares the characteristics of those with and without moderate-severe TBI .

In the first analysis, individuals were grouped based on the context in which they had suffered concussion and each of these groups were compared with those who had suffered no concussion in any category:

1. SRC group—Participants who reported concussion only in the context of sports.
2. nSRC group—Participants who reported concussion in a context other than sports.
3. Mixed concussion group—Participants who reported concussion in the context of sports and some other context.

In the second analysis, we used two variables reflecting the numbers of reported SRC and nSRC, respectively. These two variables were assessed both as categorical variables (groups 0, 1, 2 and 3+) and continuous variables.

Calculation of cognitive scores

A full description of the PROTECT study cognitive test batteries can be found in the online supplemental methods. In brief, at each wave, participants were instructed to complete each cognitive test three times at least 12 hours apart within the space of a week. The average score of the repeats was taken as the test score for that wave. Naturally, not all participants completed three repeats and in those who did there were learning effects (ie, improving performance with repetition). Therefore, in all our analyses, the number of test repeats within each wave was included as a covariate.

We used an orthogonal rotated principal components analysis (PCA) to develop cognitive domain scores using the baseline measures of 9 cognitive outcomes. Four outcomes were taken from the PROTECT Cognitive Test Battery (digit span, paired associates learning, verbal reasoning, self-ordered search) and five were measures taken from the COGTRACK assessment battery (attentional intensity index, sustained attention index, attentional fluctuation index, cognitive reaction time, memory retrieval speed) (see online supplemental methods for details). Each test score was z-transformed and winsorised to between +5 and −5 SD from the mean. The following domain scores were calculated by taking the mean of the z-transformed cognitive tests grouped by the PCA:

1. Working memory—Digit span, paired associates learning and self-ordered search.
2. Verbal reasoning—Baddeley's Grammatical Reasoning Test.
3. Processing speed—Attentional intensity index, cognitive reaction time and memory retrieval speed.
4. Attention—Sustained attention index and attentional fluctuation index.

Normality of the domain scores distribution was examined visually and numerically. If skewness was greater than 1 or less than −1, the score was transformed. The attention domain score was negatively skewed and thus was inverted, log-transformed and re-standardised to achieve a normal distribution.

Calculation of MBI score

The Mild Behavioural Impairment-Checklist (MBI-C) questionnaire is a validated 34-item list of yes/no questions grouped into five domains (decreased motivation, emotional dysregulation, impulse dyscontrol, social inappropriateness, and abnormal perception or thought content).[15] If rated 'yes', participants are asked to rate severity between 1 and 3. Our main outcome was the total MBI-C score (ie, the sum of all the MBI-C items, ranging between 0 and 102). The participant MBI-C score had a count data distribution (ie, non-normal clustering at zero with a substantial positive skew). It could not be adequately transformed, was left as a raw score and non-linear methods (negative binomial) were used in its analysis.

Statistical analysis

The analysis plan was prespecified on Open Science Framework (osf.io/nsf4b/). Baseline characteristics of each group were compared with the 'no concussion' group using Tukey's Honestly Significant Difference (HSD) and pairwise χ^2 analysis. Model construction was developed using fitting parameters Akaike information criteria and Bayesian information criteria. Given that rates of cognitive decline change with age, rather than using a simple time variable, the study used a grand mean-centred 'age at each wave' as the 'time' variable. Further, given that cognitive decline with age is non-linear, an age^2 (ie, grand mean-centred age squared) term was also included. There was considerable missing baseline covariate data particularly for physical activity and vascular risk factors (online supplemental table S5). The challenge of missing data was managed by running both partially adjusted models, including all participants, and fully adjusted models, including those with complete data, and comparing results. Partially adjusted models controlled for age, age^2, sex, education status and number of repeats in the wave and included an interaction between age and the either concussion type or concussion number. Fully adjusted models were run, controlling additionally for smoking, hypertension, stroke, coronary heart disease, diabetes, high cholesterol, history of anxiety, history of mood disorders, history of psychotic disorders, socioeconomic status and current physical activity. For details of the covariate classification, see online supplemental methods. The models specified a random intercept and slope (time varying age variable), while the other terms were treated as fixed effects. Fully adjusted models are the focus of this paper, with partially adjusted model results included in the online supplemental tables S6–S8 and discussed when discrepancies arise between fully and partially adjusted models.

Between-group differences in covariates were assessed using analysis of variance for continuous variables and χ analysis for categorical variables (see table 1). Linear mixed models were used to assess the effect of concussion type and number on cognitive scores at both baseline and on score trajectories over time. As the behavioural outcome (MBI-C) was non-normal count data, negative binomial mixed models were used to assess the effect of concussion at baseline and with increasing age. The first analysis compared the three aforementioned concussion groups (SRC, nSRC and mixed concussion) to those reporting no concussion. The second analysis assessed the effects of numbers of both lifetime SRC and nSRC numbers both as categorical (groups 1, 2, 3+, comparison group 0) and continuous variables. A number of sensitivity analyses were undertaken. First, additional models were run including a sex interaction term for the main effect and effect over time. Second, to address concerns that the concussions were either too recent to be considered chronic or too remote to be recalled correctly, we ran an analysis restricted to those who had their last concussion more than 3 months ago but less than 20 years ago.

To account for multiple comparisons (five outcomes assessed), a Sidak-corrected p value significance threshold of 0.01 was used. Statistical analyses were performed using R (V.4.3.1) using the 'lme4' and 'NBZIMM' packages.

RESULTS

Participant characteristics

Overall, there were 15 214 participants between the ages of 50 and 90 at baseline (mean age 62.7 (SD=7.2) (table 1). Of these participants, 24% were male. The average time in the study was 2.8 years (SD 1.5 years). For those who had suffered a concussion, the mean age at their first concussion was 25.5 years (SD 19.9) and the mean time since the last concussion was 29.6 years (SD 20). Those in the SRC group (57.3% male) and mixed concussion group (58% male) were substantially more likely ($p<0.001$) to be male than those in the no concussion group (19.2% male). Those in the SRC and mixed concussion groups had significantly higher levels of education ($p<0.001$ and $p=0.003$) compared with those with no concussion. There was a considerably larger portion of those in the SRC group ($p<0.001$) reporting highest level of household income and physical activity (table 1).

Cognitive and behavioural outcomes by concussion groups

At baseline, participants in the SRC group had significantly better working memory (B=0.113, 95%CI 0.038, 0.188, p=0.003) and verbal reasoning (B=0.199, 95% CI 0.092, 0.306, $p<0.001$) compared with those who had never suffered concussion in the fully adjusted model (figure 1 and table 2). This analysis controlled for education, socioeconomic status and physical activity, among other covariates. Both the non-sports-related concussion (estimate=−0.299, 95% CI−0.386 to –0.212, $p<0.001$) and mixed concussion groups (estimate=−0.316, 95% CI −0.487 to –0.144, $p<0.001$) had significantly worse MBI-C scores compared with the no concussion group in the fully adjusted model. There were no significant differences in the various groups score trajectories with increasing age.

Cognitive/behavioural outcomes and the numbers of concussions

Those who had had suffered one SRC had significantly better verbal reasoning (B=0.111, 95% CI 0.031, 0.19, p=0.006) and

Table 1 Summary of study population characteristics in comparing those with no concussion, sports-related concussion, non-sports-related concussion and mixed concussion

	Total (n=15 214)	No concussion (n=9510)	Non-sports-related concussion (n=4385)	P value	Sports-related concussion (n=514)	P value	Mixed concussion (sports+non-sports-related concussion (n=805)	P value
Mean age (SD), years	62.7 (7.2)	62.8 (7.1)	62.3 (7.3)	<0.001**	62.5 (7.5)	0.813	62.8 (7.4)	0.999
Sex (male %)	24%	19.20%	24.30%	<0.001**	57.30%	<0.001**	58%	<0.001**
Education†	1–1988 (13%)	1–1294 (13.6%)	1–561 (12.8%)	0.142	1–37 (7.2%)	<0.001**	1–96 (11.8%)	0.003**
	2–1700 (11.1%)	2–1055 (11.1%)	2–525 (11.9%)		2–52 (10.1%)		2–68 (8.4%)	
	3–3049 (20%)	3–1871 (19.6%)	3–929 (21.1%)		3–87 (16.9%)		3–162 (20%)	
	4–5143 (33.7%)	4–3243 (34%)	4–1444 (32.8%)		4–193 (37.5%)		4–263 (32.4%)	
	5–2764 (18.1%)	5–1695 (17.8%)	5–769 (17.5%)		5–118 (22.9%)		5–182 (22.4%)	
	6–609 (4%)	6–370 (3.9%)	6–171 (3.9%)		6–28 (5.4%)		6–40 (4.9%)	
Mean time in study (SD)	2.8 (1.5)	2.8 (1.5)	2.7 (1.5)	0.056	2.7 (1.5)	0.745	2.6 (1.6)	0.005**
Hypertension (%)	23.80%	23.50%	23.80%	0.747	23.70%	0.995	27.50%	0.032*
Stroke (%)	1.30%	1.20%	1.50%	0.224	1.40%	0.762	1.60%	0.384
CHD (%)	4.10%	3.60%	4.90%	0.002**	2.70%	0.374	6.20%	0.002**
Diabetes (%)	3.40%	3%	3.80%	0.027*	4.80%	0.047*	4.60%	0.034*
High Cholesterol (%)	5.70%	5.30%	6%	0.171	7.50%	0.076	6.70%	0.165
Mood disorder (%)	25.50%	23%	30.90%	<0.001**	22.10%	0.685	27.20%	0.009**
Anxiety disorder (%)	17.50%	15.90%	20.30%	<0.001**	16.70%	0.665	21.50%	<0.001**
Psychotic disorder (%)	0.30%	0.20%	0.40%	0.034*	0.20%	1	0.60%	0.025*
Smoking‡	1–7053 (54.8%)	1–4658 (57.7%)	1–1862 (49.9%)	<0.001**	1–226 (52.7%)	0.017*	1–307 (47.3%)	<0.001**
	2–5491 (42.6%)	2–3222 (39.9%)	2–1755 (47%)		2–198 (46.2%)		2–316 (48.7%)	
	3–335 (2.6%)	3–187 (2.3%)	3–117 (3.1%)		3–5 (1.2%)		3–26 (4%)	
BMI (kg/m^2)	25.2 (4.5)	25 (4.5)	25.4 (4.6)	<0.001**	25.1 (3.9)	1	25.9 (4.4)	<0.001**
Household income§	1–140 (1%)	1–75 (0.9%)	1–55 (1.4%)	0.003**	1–5 (1%)	0.001**	1–5 (0.7%)	0.507
	2–653 (4.8%)	2–385 (4.6%)	2–219 (5.6%)		2–17 (3.5%)		2–32 (4.3%)	
	3–2689 (19.9%)	3–1665 (19.9%)	3–816 (20.8%)		3–69 (14.2%)		3–139 (18.6%)	
	4–3284 (24.3%)	4–2080 (24.8%)	4–906 (23.1%)		4–114 (23.5%)		4–184 (24.7%)	
	5–3930 (29.1%)	5–2428 (29%)	5–1149 (29.3%)		5–145 (29.8%)		5–208 (27.9%)	
	6–2831 (20.9%)	6–1747 (20.8%)	6–770 (19.7%)		6–136 (28%)		6–178 (23.9%)	
Physical activity¶	1–762 (6.1%)	1–92 (1.6%)	1–45 (1.6%)	0.107	1–1 (0.3%)	0.001**	1–9 (1.7%)	0.013*
	2–3094 (24.7%)	2–1432 (25.2%)	2–727 (26%)		2–80 (23.8%)		2–105 (20%)	
	3–4666 (37.3%)	3–2318 (40.7%)	3–1054 (37.7%)		3–119 (35.4%)		3–204 (38.9%)	
	4–2585 (20.6%)	4–1177 (20.7%)	4–632 (22.6%)		4–98 (29.2%)		4–134 (25.6%)	
	5–1418 (11.3%)	5–673 (11.8%)	5–341 (12.2%)		5–38 (11.3%)		5–72 (13.7%)	
Mean no concussion (SD)	0.8 (1.5)	0 (0)	1.9 (1.6)		1.4 (1)		4 (2.4)	
Mean age first concussion (SD)	25.5 (19.9)	–	26.4 (20.2)		22.6 (16)		17.7 (13.6)	
Years since first concussion (SD)	38.6 (18.6)	–	37.5 (18.7)		41.1 (15.9)		45.6 (14)	
Mean age last concussion (SD)	35.6 (21.4)	–	36.4 (21.1)		29.7 (18.9)		37.2 (20.1)	
Years since last concussion (SD)	29.6 (20)	–	28.7 (19.8)		34.5 (18.5)		28.1 (19.1)	

The p value columns compare concussions groups to the no concussion groups. Continuous variables were compared using Tukey's HSD and the categorical variables were compared using pairwise χ^2 analysis.
*p<0.05.
†Educational status coded as follows: 1=secondary education (GSCE/O levels); 2=post-secondary education (college, A levels, NVQ3 or below); 3=vocational qualification (diploma, certificate, BTEC, NVQ4 and above or similar); 4=undergraduate degree (BA, BSc, etc); 5=post-graduate degree (MA, MSc, etc); 6=doctorate (PhD).
‡Smoking status coded as follows: 1=never smoked; 2=previous smoker; 3=current smoker.
§Household income coded as follows: 1=£0–£6000; 2=£6001–£12 000; 3=£12 001–£24 000; 4=£24 001–£36 000; 5=£36 001–£60 000; 6=more than £60 000.
¶Physical activity (episodes of exercise >20 min in the last month) coded as follows: 0=0 times; 1=1–3 times; 2=4–10 times; 3=11–20 times; 4=more than 20 times.
**p<0.01.
BMI, body mass index; CHD, coronary heart disease.

attention (B=0.115, 95% CI 0.028, 0.203, p=0.010) compared with those with no SRC at baseline (figure 1 and table 3). Those with 3+ nSRCs had significantly worse processing speed (B=−0.082, 95% CI −0.144 to –0.019, p=0.010) and attention (B=−0.156, 95% CI −0.248 to –0.063, p=0.001) compared with those with no nSRC. Additionally, in the partially adjusted analysis, those with 3+ nSRC had significantly worse working memory (B=−0.061, 95% CI −0.103 to –0.019, p=0.005), although this was not significant in the fully adjusted analysis. Those with 1 (B=−0.136, 95% CI −0.237 to –0.034, p=0.009), 2 (B=−0.322, 95% CI −0.454 to –0.189, p<0.001) or 3+ (B=−0.558, 95% CI −0.709 to –0.406, p<0.001) nSRCs had significantly worse MBI-C scores when compared with those with no nSRC. Longitudinally, those with those with 3+ nSRCs had a significantly worse trajectory of verbal reasoning with increasing age (B=−0.088, 95% CI −0.149 to −0.026, p=0.005) compared with those without nSRC. Assessing the numbers of concussion as a continuous measure, each additional nSRC was associated with progressively worse attention (B=−0.034, 95% CI −0.051 to –0.016, p<0.001) (table 4). In the partially adjusted model, nSRCs were associated with deficits in processing speed (B=−0.014, 95% CI−0.023 to –0.006, p=0.001), although this was not significant in the fully adjusted model.

Sensitivity analyses

Females who had 3+ SRC had a significantly worse trajectory of processing speed over time (B=−0.442, 95% CI −0.74 to –0.145, p=0.004) but otherwise there was no significant interactions between sex and any of the concussion type or number variables at baseline or longitudinally (online supplemental

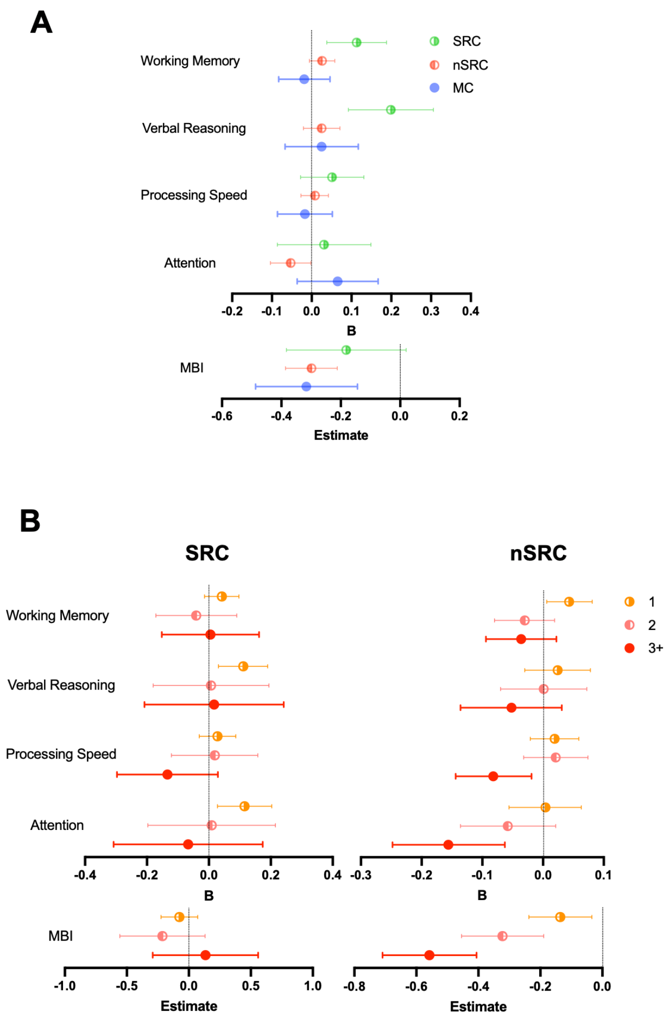

Figure 1 Results from baseline analysis of cognitive and behavioural outcomes. (A) Separating groups by concussion subgroup (sports, non-sports, mixed). The comparison group (dotted line) are those in the no concussion group. (B) Combined analysis of the effect of having 1, 2 or 3+ sports-related concussions or non-sports-related concussions. The comparison group (dotted line) are those with 0 sports-related concussions or non-sports-related concussions. MC, mixed concussion; nSRC, non-sports-related concussion; SRC, sports-related concussion.

tables S9–S11). When restricting to those with their last concussion >3 months and <20 years ago, the results were consistent, except that those in the SRC group and those with 1 SRC did not perform significantly better on any of the cognitive measures (online supplemental tables S12–S14).

DISCUSSION

This study illustrated that individuals with SRC manifested no long-term cognitive or behavioural deficits compared with those without concussion. Indeed, those who had suffered SRC had better working memory and verbal reasoning. However, this effect seemed limited to those with a single SRC. Those with two or more SRCs did not perform better on any of the cognitive or behavioural measures. Given our understanding of the pathophysiology of concussion,[16] it is clear that there is something other than the head injury itself that underlies the better cognitive outcomes in this group. It has been well demonstrated in the literature that the risks of mid-to-late-life cognitive deficits are modified by physical activity,[17] education,[18] income,[19] cardiac health[20] and smoking.[21] The SRC group had significantly better health outcomes at baseline for each of those covariates, but when controlling for these covariates, the significant differences remained, suggesting that there are unaccounted explanatory factors. One possibility is that lifetime physical activity[22] has a cumulative, greater positive impact on cognition that is not adequately captured by controlling for current physical activity, as in our model. Alternatively, involvement in sport may be associated with greater lifetime social connectivity, which is also known to be associated with lower rates of cognitive decline and dementia.[23]

Consideration of putative explanatory factors behind this difference still leaves unanswered why this study's findings are at odds with much of the SRC literature. In a systematic review, including 46 studies and 13 975 participants, Cunningham *et al*[24] examined cognitive outcomes for retired athletes. They found that retired athletes with a history of SRC had worsened outcomes in 17 of 31 (55%) of studies examining memory and 6 of 11 (55%) of studies examining executive function. They also found that 28% of studies reported a dose-response relationship, suggestive of a causative link. Our study is distinctive in the SRC literature in several ways that may explain these differences. This study examines a community-dwelling sample rather than professional athletes, and thus, the head injuries are likely less frequent, numerous and severe.

This study examines mid-to-late-life individuals who often have experienced SRC years ago, whereas most other studies of SRC focus on younger athletes in the immediate period after their head injuries when cognitive effects are likely more salient. Our study uses a behavioural measure, the MBI-C,[9] which is known to predict cognitive impairment[25–27] and dementia,[28–32] and this multipronged approach corroborates the finding that SRC is not associated with poorer long-term outcomes in this population. Interestingly, Deshpande *et al*[33] (n=3904 men, mean age=64.4) published a large study of community-dwelling individuals who played non-professional high school American Football. They found that previous footballers had no cognitive deficits and better depression scores compared with controls. Taken together, while SRC in professional athletes seems to be associated with cognitive deficits, in the general population, there are no cognitive or behavioural deficits associated with SRC.

By contrast, nSRCs were associated with worsened MBI-C scores in a dose-dependent manner and those with 3+ nSRCs had significantly worse processing speed and attention. Whereas most of the literature examining repeated concussions focuses on professional sports-related injuries, our study demonstrates that the dose-response effect is seen in non-sports-related contexts. In our previous paper,[13] we similarly found that there was a dose-response relationship between cognitive outcomes and repeated TBI. This current study suggests that the nSRC may be the more important driver in this relationship. The mechanism of injury results in differential in velocity, intensity and rotational forces,[34] which may underlie the discrepancies between nSRC and SRC outcomes. It is also likely that the sport-related physical, social and economic benefits that may offset the cognitive risks of SRC are not present in the same way for concussions associated with falls, assaults and motor vehicle accidents. Interestingly, this study showed that those with 3+ nSRCs had a worsened decline in verbal reasoning with increasing age. The effect size was small and there have not been similar findings for long-term cognitive decline within this study or in other studies,[32] and thus this result should be interpreted with caution. In our sensitivity analysis, we found that females with more than

Table 2 Summary of linear and negative binomial mixed model results examining effect of TBI subtype on cognitive/behavioural scores

	Working memory (n=7350)		Verbal reasoning (n=7350)		Processing speed (n=6767)		Attention (n=6765)		Mild behavioural impairment (n=7139)	
	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	Estimate (95% CI)	P value
Baseline										
No concussion	0	–	0	–	0	–	0	–	0	–
nSRC	0.026 (−0.006 to 0.058)	0.117	0.025 (−0.021 to 0.071)	0.294	0.008 (−0.027 to 0.042)	0.663	−0.053 (−0.104 to −0.002)	0.041*	−0.299 (−0.386 to −0.212)	**<0.001****
SRC	0.113 (0.038 to 0.188)	**0.003****	0.199 (0.092 to 0.306)	**<0.001****	0.051 (−0.028 to 0.131)	0.204	0.031 (−0.086 to 0.149)	0.599	−0.182 (−0.383 to 0.02)	0.077
Mixed concussion (nSRC+SRC)	−0.019 (−0.083 to 0.046)	0.570	0.025 (−0.067 to 0.117)	0.595	−0.017 (−0.086 to 0.052)	0.631	0.065 (−0.036 to 0.167)	0.208	−0.316 (−0.487 to −0.144)	**<0.001****
Trajectories over increasing age (5-year increments)										
Age†	0 (−0.012 to 0.011)	0.973	0.391 (0.371 to 0.411)	**<0.001****	−0.124 (−0.138 to −0.11)	**<0.001****	0.026 (0.006 to 0.046)	0.012*	0.1 (0.068 to 0.133)	**<0.001****
Age^2	−0.025 (−0.029 to −0.021)	**<0.001****	−0.049 (−0.056 to −0.043)	**<0.001****	−0.01 (−0.016 to −0.005)	**<0.001****	−0.025 (−0.034 to −0.017)	**<0.001****	−0.061 (−0.074 to −0.049)	**<0.001****
nSRC*Age	−0.009 (−0.027 to 0.01)	0.353	−0.012 (−0.045 to 0.021)	0.473	0.007 (−0.016 to 0.03)	0.579	0 (−0.034 to 0.033)	0.986	0.017 (−0.034 to 0.069)	0.510
SRC*Age	0 (−0.041 to 0.042)	0.983	−0.042 (−0.118 to 0.035)	0.284	0.028 (−0.023 to 0.08)	0.285	−0.038 (−0.113 to 0.037)	0.320	−0.024 (−0.141 to 0.092)	0.682
Mixed concussion (nSRC+SRC)*Age	0.035 (0 to 0.069)	0.052	−0.026 (−0.09 to 0.038)	0.421	−0.013 (−0.057 to 0.03)	0.544	−0.025 (−0.088 to 0.038)	0.433	−0.089 (−0.183 to 0.004)	0.062

The model was adjusted for sex, age, age^2, education, household income, smoking status, history of psychosis, history of mood disorder, history of anxiety disorder, history of hypertension, stroke, coronary heart disease, diabetes, hypercholesterolaemia and physical activity. This model compares all head injury groups to individuals in the cohort who have had no concussion, that is, a B of −0.211 at baseline means that the group had a mean score −0.211 SD lower than those with no head injuries.

*p<0.05.

**p<0.01.

†The unit of age is 5-year increments, that is, B indicates the number of SD change in cognitive score with each additional 5 years of age.

nSRC, non-sports-related concussion (ie, non-sports related); SRC, sports-related concussion.

Table 3 Summary of linear and negative binomial mixed model results examining the effect of numbers of both sports-related concussion and non-sports-related concussion (as categorical variables) on cognitive/behavioural scores

		Working memory (n=7350)		Verbal reasoning (n=7350)		Processing speed (n=6767)		Attention (n=6765)		Mild behavioural impairment (n=7139)	
		B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	Estimate (95% CI)	P value
Baseline											
nSRC	0	–	–	–	–	–	–	–	–	–	–
	1	0.043 (0.006 to 0.081)	0.024*	0.024 (−0.03 to 0.078)	0.387	0.019 (−0.021 to 0.059)	0.355	0.004 (−0.056 to 0.063)	0.903	−0.136 (−0.237 to −0.034)	**0.009****
	2	−0.03 (−0.08 to 0.019)	0.232	0.001 (−0.07 to 0.072)	0.973	0.021 (−0.032 to 0.074)	0.444	−0.058 (−0.136 to 0.021)	0.149	−0.322 (−0.454 to −0.189)	**<0.001****
	3+	−0.036 (−0.094 to 0.022)	0.229	−0.052 (−0.136 to 0.031)	0.218	−0.082 (−0.144 to −0.019)	**0.010****	−0.156 (−0.248 to −0.063)	**0.001****	−0.558 (−0.709 to −0.406)	**<0.001****
SRC	0	–	–	–	–	–	–	–	–	–	–
	1	0.042 (−0.014 to 0.097)	0.142	0.111 (0.031 to 0.19)	**0.006****	0.028 (−0.031 to 0.087)	0.360	0.115 (0.028 to 0.203)	**0.010****	−0.076 (−0.224 to 0.072)	0.312
	2	−0.041 (−0.171 to 0.09)	0.543	0.007 (−0.18 to 0.194)	0.941	0.019 (−0.121 to 0.158)	0.794	0.009 (−0.197 to 0.215)	0.929	−0.213 (−0.556 to 0.131)	0.225
	3+	0.005 (−0.152 to 0.162)	0.948	0.017 (−0.208 to 0.242)	0.882	−0.134 (−0.297 to 0.029)	0.106	−0.067 (−0.308 to 0.174)	0.586	0.134 (−0.292 to 0.559)	0.538
Trajectories over increasing age (5-year increments)											
	Age†	−0.002 (−0.013 to 0.009)	0.719	0.39 (0.37 to 0.41)	**<0.001****	−0.123 (−0.136 to to 0.109)	**<0.001****	0.025 (0.005 to 0.045)	0.013*	0.103 (0.071 to 0.134)	**<0.001****
	Age^2	−0.025 (−0.029 to to 0.021)	**<0.001****	−0.05 (−0.056 to to 0.043)	**<0.001****	−0.01 (−0.016 to −0.005)	**<0.001****	−0.026 (−0.035 to −0.017)	**<0.001****	−0.061 (−0.074 to −0.049)	**<0.001****
nSRC	1*Age	−0.011 (−0.032 to 0.011)	0.330	0.019 (−0.02 to 0.058)	0.336	0.012 (−0.015 to 0.039)	0.381	0.015 (−0.023 to 0.054)	0.438	−0.006 (−0.066 to 0.053)	0.832
	2*Age	0.012 (−0.016 to 0.04)	0.419	−0.018 (−0.069 to 0.034)	0.501	−0.023 (−0.059 to 0.012)	0.193	−0.023 (−0.075 to 0.029)	0.385	−0.02 (−0.097 to 0.057)	0.615
	3+*Age	−0.01 (−0.044 to 0.024)	0.555	−0.088 (−0.149 to −0.026)	**0.005****	0.001 (−0.042 to 0.045)	0.956	−0.019 (−0.082 to 0.044)	0.553	0.065 (−0.026 to 0.156)	0.162
SRC											
	1*Age	0.026 (−0.004 to 0.056)	0.090	−0.032 (−0.088 to 0.023)	0.256	0.008 (−0.03 to 0.045)	0.692	−0.031 (−0.085 to 0.023)	0.256	−0.059 (−0.141 to 0.023)	0.160
	2*Age	0.03 (−0.046 to 0.105)	0.444	0.135 (−0.003 to 0.273)	0.055	−0.007 (−0.105 to 0.09)	0.881	0.029 (−0.115 to 0.172)	0.696	−0.145 (−0.347 to 0.058)	0.161
	3+*Age	0.01 (−0.081 to 0.101)	0.832	−0.157 (−0.322 to 0.008)	0.063	−0.041 (−0.157 to 0.075)	0.484	−0.056 (−0.223 to 0.111)	0.511	−0.078 (−0.333 to 0.177)	0.549

The model was adjusted for sex, age, age^2, education, household income, smoking status, history of psychosis, history of mood disorder, history of anxiety disorder, history of hypertension, stroke, coronary heart disease, diabetes, hypercholesterolaemia and physical activity.
*p<0.05.
**p<0.01.
The unit of age is 5-year increments, that is, B indicates the number of SD change in cognitive score with each additional 5 years of age.
nSRC, non-sports-related concussion (ie, non-sports related); SRC, sports-related concussion.

Table 4 Summary of linear and negative binomial mixed model results examining the effect of numbers of both sports-related concussion and non-sports-related concussion (as continuous variables) on cognitive/behavioural scores

	Working memory (n=7350)		Verbal reasoning (n=7350)		Processing speed (n=6767)		Attention (n=6765)		Mild behavioural impairment (n=7139)	
	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	B (95% CI)	P value	Estimate (95% CI)	P value
Baseline										
nSRC	−0.012 (−0.023 to −0.001)	0.039*	−0.009 (−0.025 to 0.007)	0.282	−0.011 (−0.023 to 0.001)	0.072	−0.034 (−0.051 to −0.016)	**<0.001****	−0.12 (−0.15 to −0.089)	**<0.001****
SRC	0.008 (−0.018 to 0.035)	0.537	0.02 (−0.018 to 0.058)	0.297	−0.003 (−0.031 to 0.024)	0.821	0.016 (−0.025 to 0.057)	0.436	−0.003 (−0.079 to 0.073)	0.932
Trajectories over increasing age (5-year increments)										
Age	−0.003 (−0.013 to 0.008)	0.595	0.395 (0.376 to 0.413)	**<0.001****	−0.122 (−0.134 to −0.109)	**<0.001****	0.025 (0.007 to 0.044)	**0.007****	0.1 (0.071 to 0.129)	**<0.001****
Age^2	−0.024 (−0.028 to −0.02)	**<0.001****	−0.05 (−0.056 to −0.043)	**<0.001****	−0.01 (−0.016 to −0.004)	**0.001****	−0.026 (−0.034 to −0.017)	**<0.001****	−0.062 (−0.075 to −0.05)	**<0.001****
nSRC*Age	0 (−0.006 to 0.007)	0.966	−0.014 (−0.026 to −0.002)	0.023*	−0.001 (−0.009 to 0.008)	0.871	−0.003 (−0.016 to 0.009)	0.596	−0.035 (−0.077 to 0.006)	0.096
SRC*Age	0.008 (−0.007 to 0.023)	0.315	−0.011 (−0.039 to 0.017)	0.435	−0.003 (−0.022 to 0.016)	0.763	−0.014 (−0.042 to 0.013)	0.308	0.003 (−0.015 to 0.021)	0.737

Model was adjusted for sex, age, age^2, education, household income, smoking status, history of psychosis, history of mood disorder, history of anxiety disorder, history of hypertension, stroke, coronary heart disease, diabetes, hypercholesterolaemia and physical activity. This model compares all head injury groups to individuals in the cohort who have had no concussion, that is, a B of −0.211 at baseline means that the group had a mean score −0.211 SD lower than those with no head injuries.
*p<0.05.
**p<0.01.
†The unit of age is 5-year increments, that is, B indicates the number of SD change in cognitive score with each additional 5 years of age.
nSRC, non-sports-related concussion (ie, non-sports related); SRC, sports-related concussion.

three SRC had a substantially worse decline of processing speed compared with males. This may be a chance finding as no similar results were found for either the baseline analyses or for any of the other outcomes. If corroborated in future studies, this result may indicate that females are at greater risk of long-term cognitive decline from SRC. Both the aforementioned results raise the interesting possibility that even years after an injury, a history of multiple concussions may contribute to accelerated cognitive decline in some domains.

Limitations

The critical limitations of this study include its retrospective design, limitations in cognitive domains, participant dropout and unmeasured confounders. The retrospective design, with participants frequently recalling events several decades ago, may have resulted in an under-reporting of concussions and an underestimation of the effect size, particularly given that concussion is linked to memory loss. The study design may have also been affected by selection bias as males and those with cognitive deficits are less likely to participate. Because the retrospective design relies on memory to report TBI, any examination of the relationship between current memory function and concussion is confounded. As such, our study does not explore a critical cognitive domain that is known to be affected by concussion.[16] Over the course of the study, participant retention was 45.3%, which is comparable to other longitudinal studies of ageing but naturally risks confounding by survivor bias. This issue was mitigated using the linear mixed model design. Finally, as mentioned previously, unmeasured confounders such as social connectedness and lifetime physical activity may explain some of the results in this study but were not included.

CONCLUSION

To conclude, this study has found that those with SRC show no long-term cognitive or behavioural deficits compared with those without concussion. By contrast, those with nSRC showed deficits in processing speed, attention and the MBI-C, as well as a worsened rate of decline in verbal reasoning. Understanding the benefits of sport relative to the long-term risks of the injuries should inform public discourse around community level sport participation.

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America Pharm Inc, Sunovion Pharm Inc, Suven, Roche, Axosome and Biogen. CB is on Advisory Boards for the following companies: Acadia, Roche, Novo-Nordisk, AARP, Biogen and Synexus. CB received an Honorarium from Harvard University for speaking. AH is the owner and director of Future Cognition Ltd, a software development company the consulted on the development of the cognitive assessment software.

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Data availability statement Data are available upon reasonable request. Applications for the PROTECT data can be made through the following website: https://www.exeter.ac.uk/research/dementia-research/research/protect/.

ORCID iD

Matthew Joseph Lennon http://orcid.org/0000-0001-7097-3666

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Supplementary Data: Sports Related Concussion not associated with long term cognitive of behavioural deficits: The PROTECT-TBI Study

Matthew J Lennon[1,2] MD, Grant Rigney[3] MSc, Byron Creese[4,5] PhD, Dag Aarsland[6,7] PhD, Adam Hampshire[8] PhD, Clive Ballard[5] MD, Anne Corbett[5] PhD, Vanessa Raymont[2] MB ChB

1. Faculty of Medicine, University of New South Wales, Australia
2. Department of Psychiatry, University of Oxford, United Kingdom
3. Harvard Medical School, Harvard University, USA
4. Division of Psychology, Department of Life Sciences, Brunel University London, United Kingdom
5. Department of Health and Community Sciences, University of Exeter, United Kingdom
6. Department of Old age Psychiatry, IoPPN, Kings College London, United Kingdom
7. Centre for Age-related research, Stavanger University Hospital, Stavanger, Norway
8. Department of Brain Sciences, Faculty of Medicine, Imperial College London

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Supplementary Methods

Calculation of cognitive domain scores

The PROTECT Study included several batteries of cognitive tests. The PROTECT Cognitive Test Battery (PCTB) comprised the Digit Span test, Paired Associates Learning Test, Baddeley Grammatical Reasoning Test (Verbal Reasoning) and the Spatial Working Memory (Self ordered search) test. There has been 4 years of follow up for this battery. The second cognitive battery, COGTRACK, involved a number of tests assessing reaction time, processing speed, attention and delayed memory. This testing battery was ceased after 3 years of follow up.

The participants were asked to perform 3 repeats of each test at least 12 hours apart within the space of a week. The mean of the repeats was taken to be the test score for that wave. Naturally, not all participants completed three repeats. In those who did there were significant learning effects (i.e. scores improved with test repetition), thus the number of test repeats within each wave was included as a covariate in all of our analyses.

In order to develop cognitive domain scores an orthogonal rotated principal components analysis was performed on the baseline values of 9 outcome measures. Four were taken from the PCTB (Digit Span, Paired Associates Learning, Verbal Reasoning, Self-Ordered Search) and 5 were measures taken from the COGTRACK assessment battery (Attentional Intensity Index, Sustained Attention Index, Attentional Fluctuation Index, Cognitive Reaction Time, Memory Retrieval Speed).

For the main PCA the KMO test result was 0.703 and the Bartlett's Test of Sphericity p-value was <0.001 indicating an acceptable fit[33]. The tests grouped into three dimensions (see Supplementary Methods). To ensure the constructs were valid throughout the study the PCA was repeated for each wave. The tests reliably aggregated into the same groupings. Verbal Reasoning (Baddeleys Grammatical Reasoning Test) was grouped with Digit Span, Paired Associates Learning and Self-Ordered Search but did not fit conceptually within the working memory domain and thus it was analysed separately. Domain scores were calculated from the mean of the z-scores of the tests grouped by the PCA.

Each test score for all waves was standardised based on baseline mean and standard deviations. Tests in which higher scores indicated poorer performance (e.g. reaction time tests) were inverted, such that higher Z scores always indicated better performance. All Z scores were winsorized to between 5 and -5 SD from the mean.

Domain scores were calculated from the mean of the Z scores of the tests grouped by the principle components analysis. The following domain scores were computed:

1. Working Memory - Digit Span, Paired Associates Learning and Self-Ordered Search.
2. Verbal Reasoning - Baddeley's Grammatical Reasoning Test
3. Processing Speed - Attentional Intensity Index, Cognitive Reaction Time and Memory Retrieval Speed
4. Attention - Sustained Attention Index and Attentional Fluctuation Index

The domain scores were assessed for normal distribution by examining visually and testing for skewness. If the skewness was greater than 1 or less than -1 the score was transformed into a normal distribution. The attention domain score was negatively skewed and thus was inverted, log transformed and re-standardised to achieve a normal distribution.

Mild Behavioural Impairment Checklist

To reflect MBI diagnostic criteria, the MBI-C is prefixed with the following instructions to participants (with wording amended accordingly for study partner ratings): "We would like to know if there have been any subtle changes in your behavior such as changed interest in activities, altered mood, or impulsive behavior." Answer options for the questions are as follows: "Yes: the behavior has been present for at least 6 months (continuously, or on and off) and is a change from your longstanding pattern of behavior. No: behavior not present, or present for less than 6 months, no change from usual behavior. Mild: noticeable, but not a significant change. Moderate: significant, but not a dramatic change. Severe: very marked or prominent, a dramatic change."

Classification of covariates

Sex was coded as binary; 0=men, 1=women. Education was included as a 6-level ordinal variable; 1=Secondary Education, 2=Post-secondary education, 3=Vocational Qualification, 4=Undergraduate degree, 5=Post graduate degree, 6=Doctorate. Smoking was coded as a three-level variable; 0=Never smoked, 1=Previous Smoker and 2=Current Smoker. The following covariates were dummy coded: hypertension, stroke, coronary heart disease, diabetes, high cholesterol, diagnosis of anxiety disorders, diagnosis of mood disorders, and diagnosis of psychotic disorders. Household income was included as a 6-level ordinal variable (0=£0-£6,000, 1=£6,001-£12,000, 2=£12,001-£24,000, 3=£24,001-£36,000, 4=£36,001-£60,000, 5=More than £60,000). Current physical activity was coded as a 5-level ordinal variable. Participants were asked how many times in the last month they had done physical exercise lasting more then 20 minutes in which they were out of breath (0=0 times, 1=1-3 time, 2=4-10 times, 3=11-20 times, 4=more than 20 times).

Results of Principal Components analysis

	Dim.1	Dim.2	Dim.3	Dim.4	Dim.5	Dim.6	Dim.7	Dim.8	Dim.9
Digit Span	0.208	0.065	0.091	0.019	0.102	0.061	0.017	0.024	0.201
Paired Associates Learning	0.330	0.040	0.087	0.013	0.007	0.001	0.132	0.078	0.178
Verbal Reasoning	0.482	0.009	0.016	0.002	0.099	0.012	0.126	0.157	0.057
Self Ordered Search	0.249	0.072	0.051	0.004	0.207	0.086	0.001	0.060	0.051
Attentional Intensity Index	0.043	0.360	0.265	0.015	0.022	0.128	0.040	0.061	0.000
Sustained Attention Index	0.266	0.272	0.004	0.051	0.018	0.000	0.155	0.171	0.002
Attentional Fluctuation Index	0.110	0.042	0.141	0.499	0.000	0.070	0.042	0.003	0.000
Cognitive Reaction Time	0.193	0.042	0.270	0.247	0.075	0.118	0.007	0.004	0.001
Memory Retrieval Speed	0.202	0.323	0.032	0.001	0.078	0.198	0.095	0.017	0.009

Table S1 – EQUATOR-STROBE Reporting Checklist

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8 + Supplementary Methods
Bias	9	Describe any efforts to address potential sources of bias	9 + Supplementary Tables
Study size	10	Explain how the study size was arrived at	7

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8 + Supplementary Methods
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	10 + Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Table 1
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*NA*
		Cross-sectional study—Report numbers of outcome events or summary measures	*NA*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11 + Tables S2 – 4
		(*b*) Report category boundaries when continuous variables were categorized	8 + supplementary methods
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Table S2 – Comparison of those who did and did not complete the Brain Injury Screening Questionairre (BISQ)

	Completed BISQ (n=15,764)	**Did not complete BISQ (n= 4,379)**	**P**
Mean Age (SD)	62.7 (7.2)	62.2 (7.5)	**0.001****
Sex (Male %)	24.40%	27.90%	**<0.001****
Education[a]	1 - 2050 (13%) 2 - 1745 (11.1%) 3 - 3146 (20%) 4 - 5335 (33.8%) 5 - 2858 (18.1%) 6 - 629 (4%)	1 - 791 (18.1%) 2 - 522 (11.9%) 3 - 920 (21%) 4 - 1333 (30.5%) 5 - 679 (15.5%) 6 - 132 (3%)	**<0.001****
Mean Time in Study (SD)	2.8 (1.5)	1.2 (1.1)	**<0.001****
Hypertension (%)	23.90%	25.80%	0.201
Stroke (%)	1.30%	2.30%	0.017*
CHD (%)	4.10%	5.10%	0.197
Diabetes (%)	3.40%	3.80%	0.516
High Cholesterol (%)	5.70%	4.20%	0.064
Smoking[b]	1 - 7263 (54.6%) 2 - 5675 (42.7%) 3 - 359 (2.7%)	1 - 1987 (49.7%) 2 - 1828 (45.7%) 3 - 183 (4.6%)	**<0.001****
BMI (kg/m2)	25.2 (4.5)	26.1 (5.1)	**<0.001****

Table S2: Summary of study population characteristics in comparing those who had and had not completed the Brain Injury Screening Questionnaire, assessing for selection bias in those who responded to the offer to be part of the PROTECT study exploring the long term effects of head injuries. Continuous variables were compared using a student's T test and the categorical variables were compared using a Chi-Squared analysis.

[a]Educational Status coded as follows; 1=Secondary Education (GSCE/O levels), 2=Post-secondary education (College, A levels, NVQ3 or below), 3=Vocational Qualification (Diploma, certificate, BTEC, NVQ4 and above or similar), 4=Undergraduate degree (BA, BSc etc.), 5=Post graduate degree (MA, MSc, etc), 6=Doctorate (PhD)

[b]Smoking status coded as follows: 1=Never smoked, 2=Prev smoker, 3=Current smoker)

*p<0.05

**p<0.01.

Table S3 – Head injury scenario questions comprising the BISQ

Group		**Question**	**Number (% of total injuries)**	**Number (% of total participants)**
Sports-Related Concussion		…while biking? (cycling)		
		…while playing sports? (football, baseball, basketball, etc.)	1985 (15.9%)	1326 (8.7%)
non-Sports-Related Concussion	**Vehicle**	…a car/van/truck/bus crash?		
		…on a motorcycle/all-terrain vehicle?		
		.. as a pedestrian vs vehicle?	1291 (10.4%)	1067 (7%)
	Object	…from a falling object?		
		…from machinery or equipment?	1174 (9.4%)	858 (5.6%)
	Falling	…falling down stairs?		
		…falling from a high place?		
		… falling while fainting?		
		…falling while in an alcohol blackout?		
		…falling in a way otherwise mentioned?	4192 (33.7%)	2958 (19.4%)
	Outdoor Activities	…while Rollerblading/skateboarding?		
		…while horse-riding?		
		…while skiing?		
		…while on a playground?	3613 (29%)	2406 (15.8%)
	Assault	…while being assaulted or mugged?		
		…while being physically abused?		
		…while in combat (blast injury)?	1195 (9.6%)	591 (3.9%)
	Other	…head injury in another way?	1592 (12.8%)	1121 (7.3%)

Table S3: Groups for the subtypes of TBI based on the questions asked in the BISQ. Each of the above questions from the BISQ was prefaced with the statement "Have you ever had a blow to the head …." and followed the question (e.g. "…on a motorcycle/all-terrain vehicle?"). If an individual had suffered TBI of more than one category they were placed into the "Mixed group" and if an individual had suffered no concussions they were grouped into the "No concussion" group.

Table S4 - Comparison of those with and without moderate-severe TBI

	No concussion (n=9,510)	P (No concussion vs Concussion/mild TBI)	Concussion/Mild TBI (n=4,385)	P (No concussion vs moderate-severe TBI)	Moderate-severe TBI (n=510)	P (Concussion vs moderate-severe TBI)
Mean Age (SD)	62.8 (7.1)	**0.001****	62.4 (7.3)	0.94	62.9 (7.7)	0.229
Sex (Male %)	19.20%	**<0.001****	32%	**<0.001****	37.30%	0.018*
Education[a]	1 - 1294 (13.6%) 2 - 1055 (11.1%) 3 - 1870 (19.6%) 4 - 3243 (34%) 5 - 1695 (17.8%) 6 - 370 (3.9%)	0.059	1 - 694 (12.1%) 2 - 645 (11.3%) 3 - 1178 (20.6%) 4 - 1900 (33.2%) 5 - 1069 (18.7%) 6 - 239 (4.2%)	0.415	1 - 62 (12.2%) 2 - 45 (8.8%) 3 - 97 (19%) 4 - 192 (37.6%) 5 - 94 (18.4%) 6 - 20 (3.9%)	0.312
Mean Time in Study (SD)	2.8 (1.5)	**0.002****	2.7 (1.5)	0.306	2.7 (1.5)	0.975
Hypertension (%)	23.50%	0.346	24.30%	0.26	26.10%	0.452
Stroke (%)	1.20%	0.149	1.50%	**0.009****	2.80%	0.073
CHD (%)	3.60%	**0.001****	4.90%	0.033*	5.80%	0.471
Diabetes (%)	3%	**0.003****	4%	0.826	3.30%	0.585
High Cholesterol (%)	5.30%	0.043*	6.20%	0.066	7.60%	0.328
Mood disorder (%)	23%	**<0.001****	29.60%	**<0.001****	32.90%	0.139
Anxiety disorder (%)	15.90%	**<0.001****	20.20%	**<0.001****	24.90%	0.014*
Psychotic disorder (%)	0.20%	0.014	0.40%	1	0.20%	0.74
Smoking[b]	1 - 4657	**<0.001****	1 - 2395	**<0.001****	1 - 210	0.01*

	2 - 3222 3 - 187		2 – 2269 3 - 148		2 - 184 3 - 24	
BMI (kg/m2)	25 (4.5)	**<0.001****	25.5 (4.5)	0.327	25.3 (4.5)	0.842
Household Income[c]	1 - 74 (0.9%) 2 - 385 (4.6%) 3 - 1665 (19.9%) 4 - 2080 (24.8%) 5 - 2428 (29%) 6 - 1747 (20.8%)	0.082	1 - 65 (1.3%) 2 - 268 (5.2%) 3 - 1024 (19.9%) 4 - 1204 (23.4%) 5 - 1502 (29.2%) 6 - 1084 (21.1%)	**<0.001****	1 - 9 (2%) 2 - 32 (7%) 3 - 117 (25.8%) 4 - 96 (21.1%) 5 - 109 (24%) 6 - 91 (20%)	**0.006****
Mean no concussion (SD)	-	-	2.2 (1.8)	-	1.8 (2.8)	**<0.001****
Mean age 1st concussion (SD)	-	-	24.8 (19.2)	-	23.9 (17.4)	0.693
Years since 1st concussion (SD)	-	-	39.1 (18)	-	39.9 (17.1)	0.666
Mean age last concussion (SD)	-	-	35.9 (20.8)	-	36.5 (20.7)	0.872
Years since last concussion (SD)	-	-	29.2 (19.6)	-	29.5 (19.2)	0.945

Table S4: Summary of study population characteristics in comparing those with no concussion, any concussion/mild TBI, and moderate-severe TBI (who were excluded from the analysis). Continuous variables were compared using Tukey HSD and the categorical variables were compared using pairwise Chi-Squared analysis.
[a]Educational Status coded as follows; 1=Secondary Education (GSCE/O levels), 2=Post-secondary education (College, A levels, NVQ3 or below), 3=Vocational Qualification (Diploma, certificate, BTEC, NVQ4 and above or similar), 4=Undergraduate degree (BA, BSc etc.), 5=Post graduate degree (MA, MSc, etc), 6=Doctorate (PhD)
[b]Smoking status coded as follows: 1=Never smoked, 2=Prev smoker, 3=Current smoker)
[c]Household Income coded as follows: 1=£0 to £6,000, 2=£6,001 to £12,000, 3=£12,001 to £24,000, 4=£24,001 to £36,000, 5=£36,001 to £60,000, 6=More than £60,000
*p<0.05
**p<0.01.

Table S5 – Missingness of covariat data

Variable	N Missing (%)
Age	0 (0%)
Sex	0 (0%)
Education	2 (0%)
Hypertension	3122 (20.5%)
Stroke	3122 (20.5%)
CHD	3122 (20.5%)
Diabetes	3122 (20.5%)
High Cholesterol	3122 (20.5%)
Mood disorder	472 (3.1%)
Anxiety disorder	472 (3.1%)
Psychotic disorder	0 (0%)
Smoking	2376 (15.6%)
BMI (kg/m2)	316 (2.1%)
Household Income	0 (0%)
Physical activity	6202 (40.8%)

Table S5: Missingness of each of the variables included within the models

Table S6 – Cognitive/Behavioural Outcomes and Concussion groups (partially adjusted model)

	Working Memory (n=15,212)		Verbal Reasoning (n=15,212)		Processing Speed (n=11,849)		Attention (n=11,847)		Mild Behavioural Impairment (n=11,862)	
	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline										
No Concussion	-	-	-	-	-	-	-	-	-	-
nSRC	0.005 (-0.019, 0.029)	0.686	0.01 (-0.024, 0.043)	0.575	-0.01 (-0.036, 0.015)	0.429	-0.103 (-0.142, -0.064)	**<0.001 ** **	-0.414 (-0.484, -0.344)	**<0.001 ** **
SRC	0.083 (0.024, 0.142)	**0.006* ** *	0.142 (0.058, 0.226)	**0.001* ** *	0.031 (-0.033, 0.096)	0.345	0.04 (-0.057, 0.138)	0.416	-0.173 (-0.348, 0.003)	0.053
Mixed Concussion (SRC + nSRC)	-0.027 (-0.075, 0.022)	0.281	0.014 (-0.054, 0.083)	0.681	-0.02 (-0.074, 0.034)	0.463	0.019 (-0.062, 0.101)	0.643	-0.435 (-0.581, -0.289)	**<0.001 ** **
Trajectories over increasing age (5-year increments)										
Age[a]	-0.021 (-0.029, -0.013)	**<0.001 ** **	0.256 (0.242, 0.27)	**<0.001 ** **	-0.141 (-0.151, -0.131)	**<0.001 ** **	0.013 (-0.002, 0.028)	0.079	0.093 (0.066, 0.119)	**<0.001 ** **
Age^2	-0.023 (-0.026, -0.02)	**<0.001 ** **	-0.044 (-0.048, -0.039)	**<0.001 ** **	-0.009 (-0.013, -0.004)	**<0.001 ** **	-0.026 (-0.032, -0.02)	**<0.001 ** **	-0.056 (-0.066, -0.046)	**<0.001 ** **
nSRC*Age	-0.015 (-0.028, -0.001)	0.034*	0 (-0.024, 0.024)	0.996	0.01 (-0.007, 0.027)	0.252	0.003 (-0.022, 0.028)	0.826	0.033 (-0.01, 0.075)	0.136
SRC*Age	0.003 (-0.03, 0.036)	0.841	-0.019 (-0.077, 0.038)	0.511	0.044 (0.001, 0.086)	0.043	-0.039 (-0.101, 0.023)	0.219	-0.021 (-0.123, 0.081)	0.687
Mixed Concussion (SRC + nSRC)*Age	-0.001 (-0.029, 0.026)	0.916	-0.043 (-0.09, 0.005)	0.079	-0.015 (-0.049, 0.02)	0.399	-0.007 (-0.058, 0.043)	0.774	-0.028 (-0.109, 0.054)	0.505

Table S6: Summary of Linear and Negative Binomial Mixed Model results examining effect of TBI subtype on cognitive domain scores and Mild Behavioural Impairment in a model adjusted for Sex, Age, Age^2 and Education. Those in the "Sports-Related" group have only had Concussion playing active sports. The "Other" group have had Concussion in context other than playing active sport. Those in the "Mixed" group had Concussion in both sports-related and other contexts. This model compares all head injury groups to individuals in the cohort who have had no TBI i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries. The MBI-C was non-normal data and was not standardised. Results for the MBI-C are thus given as an estimate rather than a standardised B.
[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age.
*p<0.05
**p<0.01

Table S7 – Cognitive/Behavioural Outcomes and numbers of Sports-Related Concussion and non-Sports-Related Concussion (categorical) (partially adjusted model)

		Working Memory (n=15,212)		**Verbal Reasoning (n=15,212)**		**Processing Speed (n=11,849)**		**Attention (n=11,847)**		**Mild Behavioural Impairment (n=11,862)**	
		B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
						Baseline					
nSRC	**0**	-	-	-	-	-	-	-	-	-	-
	1	0.025 (-0.003, 0.053)	0.078	0 (-0.04, 0.04)	0.998	0.008 (-0.022, 0.039)	0.602	-0.044 (-0.091, 0.002)	0.058	-0.205 (-0.288, -0.122)	**<0.001****
	2	-0.03 (-0.067, 0.007)	0.110	0.029 (-0.023, 0.081)	0.278	-0.001 (-0.042, 0.039)	0.944	-0.102 (-0.163, -0.041)	**0.001****	-0.445 (-0.554, -0.336)	**<0.001****
	3+	-0.061 (-0.103, -0.019)	**0.005****	-0.063 (-0.122, -0.003)	0.039*	-0.093 (-0.141, -0.046)	**<0.001****	-0.229 (-0.301, -0.158)	**<0.001****	-0.749 (-0.873, -0.625)	**<0.001****
SRC	**0**	-	-	-	-	-	-	-	-	-	-
	1	0.019 (-0.024, 0.062)	0.384	0.073 (0.012, 0.133)	0.018*	0.022 (-0.026, 0.069)	0.366	0.104 (0.033, 0.176)	**0.004****	-0.05 (-0.178, 0.077)	0.440
	2	0.01 (-0.09, 0.111)	0.840	0.061 (-0.081, 0.202)	0.402	0.014 (-0.098, 0.127)	0.802	0.104 (-0.065, 0.273)	0.227	-0.173 (-0.473, 0.126)	0.257
	3+	0.017 (-0.101, 0.134)	0.781	-0.028 (-0.193, 0.138)	0.743	-0.088 (-0.219, 0.044)	0.191	0.003 (-0.195, 0.201)	0.977	-0.062 (-0.417, 0.293)	0.731
						Trajectories over increasing age (5-year increments)					
	Age[a]	-0.022 (-0.03, -0.014)	**<0.001****	0.257 (0.243, 0.271)	**<0.001****	-0.139 (-0.149, -0.129)	**<0.001****	0.012 (-0.003, 0.026)	0.115	0.093 (0.066, 0.119)	**<0.001****
	Age^2	-0.023 (-0.026, -0.02)	**<0.001****	-0.044 (-0.049, -0.039)	**<0.001****	-0.009 (-0.013, -0.005)	**<0.001****	-0.026 (-0.033, -0.02)	**<0.001****	-0.055 (-0.065, -0.045)	**<0.001****
nSRC	**0*Age**	-	-	-	-	-	-	-	-	-	-
	1*Age	-0.02 (-0.036, -0.004)	0.013*	0.016 (-0.012, 0.044)	0.265	0.011 (-0.009, 0.031)	0.282	0.018 (-0.011, 0.048)	0.229	0.009 (-0.042, 0.059)	0.733
	2*Age	-0.009 (-0.03, 0.013)	0.426	-0.011 (-0.048, 0.026)	0.575	-0.004 (-0.031, 0.023)	0.755	-0.01 (-0.05, 0.029)	0.610	-0.006 (-0.071, 0.059)	0.857
	3+*Age	-0.009 (-0.034, 0.016)	0.491	-0.048 (-0.091, -0.004)	0.032*	-0.008 (-0.04, 0.024)	0.620	-0.02 (-0.067, 0.027)	0.407	0.098 (0.023, 0.174)	0.011*
SRC	**0*Age**	-	-	-	-	-	-	-	-	-	-
	1*Age	0.009 (-0.015, 0.033)	0.460	-0.035 (-0.077, 0.007)	0.098	0.012 (-0.019, 0.042)	0.446	-0.02 (-0.064, 0.025)	0.387	-0.044 (-0.116, 0.028)	0.233
	2*Age	-0.003 (-0.06, 0.054)	0.906	0.013 (-0.087, 0.112)	0.804	-0.03 (-0.104, 0.045)	0.437	-0.006 (-0.115, 0.103)	0.915	-0.049 (-0.222, 0.125)	0.584
	3+*Age	0.024 (-0.046, 0.094)	0.496	-0.058 (-0.179, 0.063)	0.347	-0.016 (-0.109, 0.077)	0.735	-0.006 (-0.142, 0.13)	0.929	0.015 (-0.195, 0.226)	0.886

Table S7: Summary of Linear Mixed Model results examining effect of numbers of both Sports-Related Concussion and non-Sports-Related Concussion (as categorical variables) on cognitive domain scores in model adjusted for Sex, Age, Age^2 and Education. This model compares all head injury groups to individuals in the cohort who have had no Concussion i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries.

[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age
*p<0.05
**p<0.01

Table S8 – Cognitive/Behavioural Outcomes and numbers of Sports-Related Concussion and non-Sports-Related Concussion (continuous) (partially adjusted model)

	Working Memory (n=15,212)		**Verbal Reasoning (n=15,212)**		**Processing Speed (n=11,849)**		**Attention (n=11,847)**		**Mild Behavioural Impairment (n=11,862)**	
	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline										
nSRC	-0.013 (-0.021, -0.005)	**0.001****	0.006 (-0.021, 0.033)	0.647	-0.014 (-0.023, -0.006)	**0.001****	-0.052 (-0.065, -0.039)	**<0.001****	-0.163 (-0.188, -0.138)	**<0.001****
SRC	0.007 (-0.012, 0.026)	0.495	-0.006 (-0.017, 0.005)	0.277	0.003 (-0.019, 0.024)	0.815	0.031 (-0.001, 0.063)	0.060	-0.007 (-0.066, 0.051)	0.808
Trajectories over increasing age (5-year increments)										
Age[a]	-0.025 (-0.032, -0.017)	**<0.001****	0.26 (0.247, 0.272)	**<0.001****	-0.138 (-0.147, -0.129)	**<0.001****	0.013 (0, 0.027)	0.053	0.094 (0.069, 0.118)	**<0.001****
Age^2	-0.023 (-0.026, -0.02)	**<0.001****	-0.044 (-0.049, -0.039)	**<0.001****	-0.009 (-0.013, -0.004)	**<0.001****	-0.026 (-0.032, -0.02)	**<0.001****	-0.056 (-0.066, -0.046)	**<0.001****
nSRC*Age	-0.003 (-0.008, 0.001)	0.153	-0.009 (-0.017, -0.001)	0.037*	-0.001 (-0.007, 0.005)	0.772	-0.003 (-0.012, 0.006)	0.533	-0.008 (-0.04, 0.024)	0.623
SRC*Age	0.004 (-0.007, 0.015)	0.517	-0.008 (-0.027, 0.011)	0.422	0.001 (-0.013, 0.015)	0.872	-0.006 (-0.026, 0.015)	0.599	0.007 (-0.008, 0.021)	0.363

Table S8: Summary of Linear Mixed Model results examining effect of numbers of both Sports-Related Concussion (SRC) and non-Sports-Related Concussion (nSRC) (as continuous variables) on cognitive domain scores in model adjusted for Sex, Age, Age^2 and Education. This model compares all head injury groups to individuals in the cohort who have had no Concussion i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries.

[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age

*p<0.05

**p<0.01

Table S9 – Cognitive/Behavioural Outcomes and Concussion groups (fully adjusted model) including sex interaction

	Working Memory (n=7,350)		Verbal Reasoning (n=7,350)		Processing Speed (n=6,767)		Attention (n=6,765)		Mild Behavioural Impairment (n=7,139)	
	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline										
Sex (Female)	-0.121 (-0.168, -0.074)	**<0.001 ****	0.006 (-0.062, 0.074)	0.854	-0.048 (-0.098, 0.002)	0.059	0.071 (-0.003, 0.144)	0.061	0.427 (0.298, 0.556)	**<0.001 ****
No Concussion*Sex	0	-	0	-	0	-	0	-	1	-
nSRC*Sex	0.029 (-0.047, 0.106)	0.451	0.003 (-0.107, 0.112)	0.963	0.026 (-0.055, 0.106)	0.536	0.05 (-0.07, 0.17)	0.411	-0.076 (-0.281, 0.129)	0.468
SRC*Sex	-0.106 (-0.257, 0.045)	0.168	-0.038 (-0.254, 0.179)	0.732	0.09 (-0.07, 0.25)	0.271	0.236 (-0.002, 0.473)	0.052	-0.093 (-0.5, 0.315)	0.655
Mixed Concussion (SRC + nSRC)*Sex	0.006 (-0.125, 0.136)	0.930	-0.086 (-0.274, 0.101)	0.366	0.022 (-0.119, 0.162)	0.763	0.081 (-0.127, 0.29)	0.443	0.163 (-0.186, 0.513)	0.360
Trajectories over increasing age (5-year increments)										
Sex	-0.086 (-0.13, -0.041)	**<0.001 ****	0.25 (0.16, 0.339)	**<0.001 ****	-0.022 (-0.07, 0.025)	0.358	0.139 (0.072, 0.205)	**<0.001 ****	-0.322 (-0.438, -0.205)	**<0.001 ****
Age[a]	-0.019 (-0.043, 0.005)	0.117	0.336 (0.292, 0.379)	**<0.001 ****	-0.135 (-0.164, -0.107)	**<0.001 ****	-0.008 (-0.05, 0.034)	0.707	-0.08 (-0.148, -0.013)	0.020*
Age^2	-0.024 (-0.028, -0.02)	**<0.001 ****	-0.048 (-0.054, -0.041)	**<0.001 ****	-0.01 (-0.016, -0.005)	**0.001* ***	-0.024 (-0.033, -0.015)	**<0.001 ****	0.06 (0.048, 0.073)	**<0.001 ****
Age*Sex	0.023 (-0.003, 0.049)	0.079	0.07 (0.023, 0.118)	**0.004* ***	0.014 (-0.018, 0.046)	0.386	0.042 (-0.004, 0.089)	0.075	-0.023 (-0.098, 0.051)	0.537
nSRC*Age	0.003 (-0.039, 0.046)	0.881	-0.029 (-0.108, 0.049)	0.463	-0.033 (-0.086, 0.02)	0.224	-0.011 (-0.089, 0.067)	0.78	-0.049 (-0.168, 0.07)	0.423
SRC*Age*Sex	-0.005 (-0.091, 0.081)	0.916	-0.017 (-0.176, 0.141)	0.829	-0.064 (-0.171, 0.042)	0.238	0.016 (-0.139, 0.171)	0.839	-0.254 (-0.498, -0.01)	0.041*
Mixed Concussion (SRC+nSRC)*Age*Sex	-0.028 (-0.102, 0.046)	0.457	-0.001 (-0.137, 0.134)	0.984	-0.057 (-0.15, 0.035)	0.224	-0.004 (-0.138, 0.131)	0.955	0.211 (0.011, 0.412)	0.039*

Table S9: Summary of Linear Mixed Model results examining effect of Concussion subtype on cognitive domain scores with interaction between Concussion group and Sex. The model is adjusted for Sex, Age, Age^2, Education, household income, smoking status, history of psychosis, history of mood disorder, history of anxiety disorder, history of hypertension, stroke, coronary heart disease, diabetes, hypercholesterolaemia and physical activity.

*p<0.05

**p<0.01

Table S10 – Cognitive/Behavioural Outcomes and numbers of Sports-Related Concussion and non-Sports-Related Concussion (categorical) (fully adjusted model) including sex interaction

		Working Memory (n=7,350)		**Verbal Reasoning (n=7350)**		**Processing Speed (n=6767)**		**Attention (n=6,765)**		**Mild Behavioural Impairment (n=7139)**	
		B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline											
	Sex	-0.134 (-0.18, -0.089)	**<0.001****	-0.003 (-0.068, 0.063)	0.933	-0.047 (-0.095, 0.001)	0.054	0.089 (0.018, 0.16)	0.015*	0.423 (0.299, 0.547)	**<0.001****
nSRC	**0*Sex**										
	1*Sex	0.064 (-0.021, 0.148)	0.139	-0.011 (-0.132, 0.109)	0.852	0.013 (-0.076, 0.101)	0.778	-0.046 (-0.177, 0.086)	0.494	-0.01 (-0.236, 0.216)	0.932
	2*Sex	0.011 (-0.101, 0.123)	0.846	0.066 (-0.094, 0.226)	0.417	0.024 (-0.094, 0.142)	0.689	0.049 (-0.126, 0.224)	0.585	-0.215 (-0.513, 0.082)	0.156
	3+*Sex	0.136 (0.01, 0.262)	0.034*	0.068 (-0.113, 0.249)	0.461	0.043 (-0.091, 0.178)	0.529	0.083 (-0.116, 0.283)	0.413	0.014 (-0.313, 0.34)	0.934
SRC	**0*Sex**										
	1*Sex	-0.08 (-0.192, 0.031)	0.156	-0.11 (-0.269, 0.05)	0.178	0.018 (-0.101, 0.136)	0.770	0.132 (-0.044, 0.307)	0.142	0.048 (-0.249, 0.345)	0.751
	2*Sex	-0.045 (-0.339, 0.248)	0.761	-0.085 (-0.507, 0.336)	0.691	0.079 (-0.245, 0.402)	0.634	-0.224 (-0.703, 0.255)	0.359	0.071 (-0.713, 0.855)	0.859
	3+*Sex	-0.098 (-0.522, 0.325)	0.649	0.204 (-0.404, 0.812)	0.511	0.006 (-0.429, 0.441)	0.979	0.069 (-0.575, 0.713)	0.833	0.565 (-0.599, 1.729)	0.342
Trajectories over increasing age (5-year increments)											
	Sex	-0.099 (-0.142, -0.056)	**<0.001****	0.242 (0.156, 0.327)	**<0.001****	-0.019 (-0.065, 0.026)	0.41	0.153 (0.089, 0.217)	**<0.001****	-0.322 (-0.434, -0.211)	**<0.001****
	Age[a]	-0.025 (-0.047, -0.002)	0.035*	0.337 (0.296, 0.379)	**<0.001****	-0.129 (-0.156, -0.101)	**<0.001****	-0.007 (-0.047, 0.033)	0.741	-0.067 (-0.131, -0.002)	0.043*
	Age^2	-0.024 (-0.028, -0.02)	**<0.001****	-0.048 (-0.055, -0.041)	**<0.001****	-0.011 (-0.017, -0.005)	**<0.001****	-0.024 (-0.033, -0.016)	**<0.001****	0.06 (0.047, 0.073)	**<0.001****
	Sex*Age	0.028 (0.003, 0.053)	0.029*	0.068 (0.022, 0.114)	**0.004****	0.008 (-0.023, 0.039)	0.618	0.041 (-0.004, 0.085)	0.077	-0.044 (-0.116, 0.027)	0.225
nSRC	**0*Age*Sex**										
	1*Age*Sex	0.01 (-0.036, 0.057)	0.668	0.008 (-0.078, 0.094)	0.863	-0.01 (-0.068, 0.048)	0.733	-0.024 (-0.108, 0.06)	0.576	0.02 (-0.097, 0.137)	0.738
	2*Age*Sex	-0.031 (-0.094, 0.032)	0.339	-0.04 (-0.155, 0.074)	0.489	-0.037 (-0.115, 0.042)	0.359	0.027 (-0.088, 0.141)	0.647	0.132 (-0.093, 0.356)	0.251
	3+*Age*Sex	-0.043 (-0.117, 0.03)	0.246	-0.087 (-0.22, 0.047)	0.203	0.01 (-0.083, 0.103)	0.827	0.027 (-0.108, 0.162)	0.694	-0.019 (-0.313, 0.275)	0.897
SRC	**0*Age*Sex**										
	1*Age*Sex	-0.01 (-0.072, 0.052)	0.744	0.033 (-0.081, 0.147)	0.57	-0.023 (-0.1, 0.053)	0.552	0.017 (-0.095, 0.128)	0.77	-0.042 (-0.148, 0.065)	0.446
	2*Age*Sex	-0.009 (-0.211, 0.193)	0.929	0.016 (-0.334, 0.365)	0.93	-0.151 (-0.476, 0.173)	0.361	0.154 (-0.326, 0.635)	0.529	0.071 (-0.073, 0.216)	0.332
	3+*Age*Sex	-0.114 (-0.36, 0.131)	0.36	-0.219 (-0.662, 0.224)	0.333	-0.442 (-0.74, -0.145)	**0.004****	-0.282 (-0.709, 0.144)	0.194	-0.028 (-0.187, 0.131)	0.727

Table S10: Summary of Linear Mixed Model results examining effect of numbers of both Sports-Related Concussion (SRC) and non-Sports-Related Concussion (nSRC) (as categorical variables) on cognitive domain scores with interaction for sex. The model is adjusted for Sex, Age, Age^2, Education, household income, smoking status, history of psychosis, history of mood disorder, history of anxiety disorder, history of

hypertension, stroke, coronary heart disease, diabetes, hypercholesterolaemia and physical activity. This model compares all head injury groups to individuals in the cohort who have had no Concussion i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries.
[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age
*p<0.05
**p<0.01

Table S11 – Cognitive/Behavioural Outcomes and numbers of Sports-Related Concussion and non-Sports-Related Concussion (continuous) (fully adjusted model) including sex interaction

	Working Memory (n=7,350)		**Verbal Reasoning (n=7,350**		**Processing Speed (n=6,767)**		**Attention (n=6,765)**		**Mild Behavioural Impairment (n=7,139)**	
	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline										
Sex	-0.138 (-0.178, -0.099)	<0.001	-0.034 (-0.091, 0.023)	0.242	-0.047 (-0.089, -0.005)	0.028*	0.061 (-0.001, 0.123)	0.053	0.431 (0.322, 0.539)	<0.001
nSRC*Sex	0.022 (-0.002, 0.045)	0.074	0.021 (-0.013, 0.054)	0.231	0.004 (-0.021, 0.03)	0.730	0.029 (-0.008, 0.066)	0.128	-0.015 (-0.078, 0.048)	0.642
SRC*Sex	-0.014 (-0.078, 0.051)	0.679	0.034 (-0.058, 0.126)	0.470	0.038 (-0.031, 0.107)	0.276	0.082 (-0.02, 0.184)	0.115	-0.013 (-0.194, 0.169)	0.892
Trajectories over increasing age (5-year increments)										
Sex	-0.106 (-0.143, -0.069)	**<0.001 ****	0.21 (0.137, 0.284)	**<0.001 ****	-0.02 (-0.059, 0.02)	0.326	0.123 (0.068, 0.178)	**<0.001 ****	-0.366 (-0.461, -0.272)	**<0.001 ****
Age[a]	-0.024 (-0.043, -0.004)	0.02*	0.339 (0.303, 0.375)	**<0.001 ****	-0.123 (-0.147, -0.099)	**<0.001 ****	-0.005 (-0.04, 0.03)	0.783	-0.07 (-0.125, -0.015)	0.013*
Age^2	-0.024 (-0.028, -0.02)	**<0.001 ****	-0.048 (-0.055, -0.041)	**<0.001 ****	-0.01 (-0.016, -0.005)	**0.001****	-0.024 (-0.033, -0.015)	**<0.001 ****	0.061 (0.048, 0.073)	**<0.001 ****
Age*Sex	0.026 (0.005, 0.048)	0.018*	0.075 (0.035, 0.115)	**<0.001 ****	0.003 (-0.024, 0.03)	0.832	0.038 (-0.001, 0.078)	0.057	-0.039 (-0.101, 0.022)	0.212
nSRC*Age*Sex	-0.006 (-0.02, 0.008)	0.386	-0.017 (-0.042, 0.008)	0.188	-0.002 (-0.019, 0.016)	0.853	0.007 (-0.019, 0.032)	0.604	0.053 (-0.052, 0.158)	0.322
SRC*Age*Sex	-0.004 (-0.042, 0.034)	0.835	-0.013 (-0.083, 0.056)	0.706	-0.049 (-0.097, -0.001)	0.046*	-0.012 (-0.082, 0.057)	0.733	-0.004 (-0.041, 0.033)	0.827

Table S11: Summary of Linear Mixed Model results examining effect of numbers of both Sports-Related Concussion and nSRC (as continuous variables) on cognitive domain scores with interaction for Sex. The model is adjusted for Sex, Age, Age^2, Education, household income, smoking status, history of psychosis, history of mood disorder, history of anxiety disorder, history of hypertension, stroke, coronary heart disease, diabetes, hypercholesterolaemia and physical activity. This model compares all head injury groups to individuals in the cohort who have had no Concussion i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries.
[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age

*p<0.05
**p<0.01

Table S12 – Cognitive/Behavioural Outcomes and Concussion groups (partially adjusted model) with last reported TBI >3 months and <20 years in the past.

	Working Memory (n=12,538)		Verbal Reasoning (n=12,535)		Processing Speed (n=9,852)		Attention (n=9,850)		Mild Behavioural Impairment (n=12,341)	
	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline										
No Concussion	0	-	0	-	0	-	0	-	1	-
nSRC	-0.004 (-0.032, 0.024)	0.789	-0.01 (-0.05, 0.029)	0.619	-0.009 (-0.039, 0.022)	0.586	-0.105 (-0.151, -0.058)	**<0.001 ****	-0.48 (-0.563, -0.398)	**<0.001 ****
SRC	0.02 (-0.063, 0.102)	0.641	0.072 (-0.044, 0.188)	0.221	0.011 (-0.078, 0.101)	0.806	-0.067 (-0.203, 0.069)	0.333	-0.238 (-0.484, 0.008)	0.058
Mixed Concussion (SRC + nSRC)	-0.053 (-0.116, 0.011)	0.105	0.013 (-0.076, 0.103)	0.771	-0.056 (-0.128, 0.016)	0.130	-0.002 (-0.111, 0.107)	0.976	-0.443 (-0.634, -0.252)	**<0.001 ****
Trajectories over increasing age (5-year increments)										
Age[a]	-0.022 (-0.03, -0.013)	**<0.001 ****	0.261 (0.247, 0.276)	**<0.001 ****	-0.14 (-0.15, -0.13)	**<0.001 ****	0.014 (-0.001, 0.03)	0.068	0.085 (0.057, 0.113)	**<0.001 ****
Age^2	-0.022 (-0.025, -0.019)	**<0.001 ****	-0.043 (-0.049, -0.038)	**<0.001 ****	-0.01 (-0.014, -0.005)	**<0.001 ****	-0.026 (-0.033, -0.019)	**<0.001 ****	-0.058 (-0.069, -0.047)	**<0.001 ****
nSRC*Age	-0.016 (-0.033, 0)	0.046*	-0.012 (-0.04, 0.017)	0.413	0.003 (-0.017, 0.024)	0.758	-0.003 (-0.033, 0.027)	0.829	0.056 (0.006, 0.106)	0.027*
SRC*Age	-0.01 (-0.058, 0.037)	0.675	-0.064 (-0.148, 0.019)	0.133	0.066 (0.005, 0.127)	0.033*	-0.031 (-0.121, 0.058)	0.496	0.002 (-0.145, 0.148)	0.982
Mixed Concussion (SRC+nSRC)*Age	-0.006 (-0.042, 0.029)	0.720	-0.076 (-0.138, -0.013)	0.018*	-0.026 (-0.07, 0.018)	0.252	-0.003 (-0.068, 0.062)	0.929	-0.031 (-0.134, 0.071)	0.550

Table S12: Summary of Linear and Negative Binomial Mixed Model results examining effect of TBI subtype on cognitive domain scores restricting to those with last reported TBI >3 months and <20 years in the past. Model were adjusted for Sex, Age, Age^2 and Education. This model compares all head injury groups to individuals in the cohort who have had no TBI i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries.

[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age

*p<0.05

**p<0.01

Table S13 – Cognitive/Behavioural Outcomes and numbers of Sports-Related Concussion and non-Sports-Related Concussion (categorical) (partially adjusted model) with last reported TBI >3 months and <20 years in the past.

		Working Memory (n=12,538)		**Verbal Reasoning (n=12,535)**		**Processing Speed (n=9,852)**		**Attention (n=9,850)**		**Mild Behavioural Impairment (n=12,341)**	
		B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
						Baseline					
nSRC	**0**										
	1	0.014 (-0.021, 0.048)	0.437	-0.021 (-0.07, 0.027)	0.391	-0.001 (-0.038, 0.037)	0.975	-0.015 (-0.072, 0.042)	0.609	-0.294 (-0.396, -0.192)	**<0.001 ****
	2	-0.025 (-0.072, 0.022)	0.303	0.048 (-0.019, 0.114)	0.159	0.01 (-0.042, 0.062)	0.708	-0.142 (-0.221, -0.064)	**<0.001 ****	-0.424 (-0.562, -0.285)	**<0.001 ****
	3+	-0.045 (-0.096, 0.006)	0.081	-0.068 (-0.14, 0.003)	0.061	-0.073 (-0.13, -0.016)	0.012*	-0.233 (-0.319, -0.147)	**<0.001 ****	-0.811 (-0.959, -0.663)	**<0.001 ****
SRC	**0**										
	1	-0.026 (-0.084, 0.032)	0.378	0.043 (-0.039, 0.125)	0.300	-0.027 (-0.092, 0.038)	0.420	0.05 (-0.048, 0.148)	0.319	-0.033 (-0.207, 0.141)	0.710
	2	0.012 (-0.124, 0.148)	0.864	0.091 (-0.1, 0.282)	0.350	0.072 (-0.079, 0.222)	0.351	0.062 (-0.164, 0.289)	0.590	-0.148 (-0.542, 0.247)	0.463
	3+	0.01 (-0.148, 0.169)	0.897	0.021 (-0.203, 0.245)	0.855	-0.073 (-0.254, 0.109)	0.433	-0.019 (-0.292, 0.255)	0.894	-0.046 (-0.531, 0.438)	0.851
						Trajectories over increasing age (5-year increments)					
	Age[a]	-0.022 (-0.031, -0.014)	**<0.001 ****	0.261 (0.247, 0.275)	**<0.001 ****	-0.139 (-0.149, -0.128)	**<0.001 ****	0.014 (-0.001, 0.029)	0.072	0.086 (0.059, 0.114)	**<0.001 ****
	Age^2	-0.022 (-0.025, -0.019)	**<0.001 ****	-0.043 (-0.049, -0.038)	**<0.001 ****	-0.01 (-0.015, -0.005)	**<0.001 ****	-0.026 (-0.033, -0.02)	**<0.001 ****	-0.058 (-0.069, -0.047)	**<0.001 ****
nSRC	**0*Age**										
	1*Age	-0.014 (-0.034, 0.005)	0.155	0.015 (-0.02, 0.049)	0.412	0.014 (-0.011, 0.039)	0.270	0.009 (-0.027, 0.045)	0.622	0.05 (-0.011, 0.112)	0.111
	2*Age	-0.016 (-0.043, 0.011)	0.237	-0.043 (-0.09, 0.005)	0.078	-0.017 (-0.051, 0.017)	0.335	-0.023 (-0.073, 0.028)	0.376	-0.041 (-0.122, 0.04)	0.322
	3+*Age	-0.02 (-0.051, 0.01)	0.189	-0.048 (-0.101, 0.006)	0.079	-0.036 (-0.075, 0.003)	0.072	-0.013 (-0.07, 0.044)	0.662	0.132 (0.043, 0.221)	**0.004****
SRC	**0*Age**										
	1*Age	0.004 (-0.029, 0.037)	0.798	-0.063 (-0.122, -0.005)	0.034	0.027 (-0.014, 0.068)	0.198	-0.012 (-0.072, 0.048)	0.695	-0.056 (-0.155, 0.042)	0.261
	2*Age	-0.013 (-0.086, 0.059)	0.715	-0.043 (-0.173, 0.088)	0.521	-0.037 (-0.129, 0.055)	0.432	0.015 (-0.12, 0.15)	0.829	-0.029 (-0.236, 0.179)	0.787
	3+*Age	0.014 (-0.084, 0.112)	0.782	-0.059 (-0.229, 0.111)	0.498	-0.083 (-0.23, 0.064)	0.268	0.056 (-0.16, 0.272)	0.609	-0.003 (-0.299, 0.292)	0.982

Table S13: Summary of Linear Mixed Model results examining effect of numbers of both Sports-Related Concussion (SRC) and non-Sports-Related Concussion (nSRC) (as categorical variables) on cognitive domain scores restricting to those with last reported TBI >3 months and <20 years in the past. Models were adjusted for Sex, Age, Age^2 and Education. This model compares all head injury groups to individuals in the cohort who have had no Concussion i.e. a B of -0.211 at baseline means that the group had a mean score -0.211 standard deviations lower than those with no head injuries.

[a]The unit of age is 5 year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age

*p<0.05

**p<0.01

Table S14 – Cognitive/Behavioural Outcomes and numbers of Sports-Related Concussion and non-Sports-Related Concussion (continuous) (partially adjusted model) with last reported TBI >3 months and <20 years in the past.

	Working Memory (n=12,538)		**Verbal Reasoning (n=12,535)**		**Processing Speed (n=9,852)**		**Attention (n=9,850)**		**Mild Behavioural Impairment (n=12,341)**	
	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	B (95 CI)	P	Estimate (95 CI)	P
Baseline										
nSRC	-0.01 (-0.019, -0.001)	0.036*	-0.004 (-0.018, 0.009)	0.514	-0.012 (-0.023, -0.002)	0.023*	-0.051 (-0.067, -0.035)	**<0.001 ****	-0.174 (-0.204, -0.144)	**<0.001 ****
SRC	-0.002 (-0.028, 0.024)	0.867	0.01 (-0.027, 0.047)	0.590	0.004 (-0.026, 0.034)	0.780	0.014 (-0.031, 0.06)	0.531	0.008 (-0.075, 0.092)	0.843
Trajectories over increasing age (5-year increments)										
Age[a]	-0.023 (-0.031, -0.015)	**<0.001 ****	0.262 (0.248, 0.276)	**<0.001 ****	-0.137 (-0.147, -0.127)	**<0.001 ****	0.013 (-0.002, 0.027)	0.081	0.091 (0.066, 0.117)	**<0.001 ****
Age^2	-0.022 (-0.025, -0.019)	**<0.001 ****	-0.043 (-0.049, -0.038)	**<0.001 ****	-0.01 (-0.015, -0.005)	**<0.001 ****	-0.026 (-0.033, -0.019)	**<0.001 ****	-0.059 (-0.07, -0.048)	**<0.001 ****
nSRC*Age	-0.006 (-0.012, -0.001)	0.033*	-0.012 (-0.022, -0.002)	0.020*	-0.005 (-0.013, 0.002)	0.170	-0.002 (-0.013, 0.009)	0.785	-0.002 (-0.047, 0.043)	0.927
SRC*Age	0 (-0.015, 0.016)	0.969	-0.021 (-0.047, 0.006)	0.134	0.004 (-0.017, 0.024)	0.739	0.002 (-0.029, 0.032)	0.916	0.009 (-0.008, 0.026)	0.308

Table S14: Summary of Linear Mixed Model results examining effect of numbers of both Sports-Related Concussion (SRC) and non-Sports-Related Concussion (nSRC) (as continuous variables) on cognitive domain scores. The models were adjusted for Sex, Age, Age^2 and Education. This model assesses the effect of each additional Concussion on cognitive outcomes i.e. a B of -0.051 at baseline means that each additional Concussion reported by the individual was associated with a 0.051 SD lower cognitive score compared to those with no reported Concussion.

[a]The unit of age is 5-year increments i.e. the B indicates the number of standard deviations change in cognitive score with each additional 5 years of age

*p<0.05

******p<0.01