# The association between participation in high-impact contact sports and development of young-onset dementia: A narrative systematic review

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**Key-Words:** young-onset dementia; contact sport; football; soccer, NFL, mild traumatic brain injury.

**Key Points:**

1. Current research on the association between sport participation and dementia may often omit data that is representative of dementia at young ages.
2. In this review, seven out of eight studies showed higher risk of young-onset dementia in athletes and four studies were statistically significant.
3. But only two sports were able to be represented in eligible studies: American Football and Association Football (soccer).
4. Other demographics also tend not to be considered in this research, including female athletes.

## Abstract

**Background:** There is growing concern that repetitive brain injury from high impact sports participation may be a risk factor for dementia, and brain injury has been linked to younger age of dementia onset. People with young-onset dementia often have unique needs and challenges, requiring support that is tailored to their age and interests; therefore it is important for collision sporting worlds to have insight into whether young-onset dementia risk is an area of concern for their alumni. The aim of this review was to evaluate observational studies to ascertain the nature of association for young onset dementia and high impact contact sports in current empirical literature.

**Method:** Five databases were searched up to November 2025 with terms covering sports associated with concussion risk, including a wide variety of combat sports, team based high-impact and collision sports, and individual sports associated with high concussion risk, along with progressive neurodegenerative pathologies and as terminologies relating to concussion. Studies were eligible for inclusion if they included a measurement of a clinically diagnosable dementia in their samples and participants associated with a high impact contact sport. Analysis grouped studies based on comparability to young-onset dementia, either directly (group 1) or through a mean age below 65 (group 2). Due to heterogeneity of study methodology, a narrative synthesis was adopted to report the findings of the review.

**Results:** Eight studies were eligible for inclusion, consisting of 7,385 participants. Studies largely focused on soccer and American football, but cycling and ice-hockey were included in two studies. Most studies identified dementia through self-reporting (n=5), but telephone assessment alongside self-report (n=1), and assessment of medical and death records (n=2) were also utilised. NFL (National Football League) players may be at an increased risk of developing dementia at younger ages compared to the general population. Findings on association football were suggestive of an increased risk of dementia for younger people; however, a sensitivity analysis suggested this evidence is not consistent.

**Conclusions:** Existing evidence on the impact of sport-related brain injury and young-onset dementia is very limited to date. The sport and dementia literature may not be reflective of the experiences of those aged below 65. Future research should place

emphasis on the concern around athletes at a young age reporting dementia diagnosis, as well as considering additional sports, countries, and demographics.

## 1. Background

Young-onset dementia refers to the onset of dementia before 65 years [1]. It accounts for around 7-9% of all dementia cases [2], however prevalence estimates may be under-reported due to long diagnosis times and limited methods of collecting health data [3]. The impact of young-onset dementia can differ from late-onset dementia in a variety of ways, there can be greater psycho-social impacts relating to finances and employment [4] and often leads to disruption in family relationships [5]. Young-onset dementia has also been associated with increased depressive symptoms [6] and suicide risk without timely support [7].

A complex clinical presentation can make defining the causes of young-onset dementia a challenging process [8]. There is an increased heterogeneity of conditions involving many different pathologies, and it may be more likely to present secondarily to other diseases. This complexity may be related to an increase in genetic risk factors, and there are known mutations that have been attributed to rare forms of dementias [9]. Heritability has been shown to be minimal however [10], and a study focusing on people under the age of 45, despite finding a stronger genetic basis, concluded that 18% of dementias had no known origin [11]. This has led to a growing interest in the presence of modifiable, environmental risk factors for young-onset dementia, which have highlighted potential associations with cardio-vascular issues, psychiatric issues, heavy alcohol use, and social isolation among others [12,13].

Traumatic brain injury (TBI) is considered an established risk factor for dementia and may play a more prominent role for those under sixty-five. A review of modifiable risk factors for dementia concluded that TBI is a particularly important consideration for younger people with dementia [14], and a systematic review on dementia risk factors found a higher risk of dementia in TBI patients under 65 compared to those over sixty-five [15]. Studies assessing TBI and young onset dementia association are sparse and inconsistent, however increased risks of Alzheimer's disease and fronto-temporal dementia have been detailed in 9/11 veterans who experienced head trauma [16], and military veterans [17]. A recent systematic review of modifiable risk factors for young-onset dementia identified traumatic brain injury and repeated traumatic brain injury (rTBI) as having potential causal roles which may counter-act a protective role of physical activity [18], however in another study, no TBI effect of any kind was found [19]. It is likely that attributing head injury as a risk factor due to brain injury is complicated by various methodological concerns, including issues in defining severity, particularly with emerging concerns around sub-concussive impacts [20]. Additionally, the absolute risk of young-onset dementia through TBI may be low, requiring high powered studies to identify. To assist with these issues, more context-specific research is required from which the nature and frequency of head trauma can be accurately identified.

Sports offers some advantages to this research as it can allow for identification of head traumas through official reports and may potentially allow stratification between different severities of brain injury. Systematic reviews have highlighted high incidence of concussion from many sports including rugby, soccer, American football, lacrosse, and ice-hockey [21], cycling [22], and recent reviews have revealed high incidence in the professional boxing [23,24]. Given that each sport may also provide different causes of head trauma, e.g. heading footballs or loss of consciousness in boxing, it provides a foundation for assessing the complexities of its long-term impact. This has been explored in systematic reviews on sports participation and long-term cognitive impairment [25], as well as reviews exploring sports-related neurodegenerative cause of death [26]. To date, no review has concentrated on the risks across different sports specifically for young-onset dementia.

The focus of this systematic review was to explore associations between high impact contact sports participation and clinically diagnosable dementia for those aged <65years. The review focused on observational studies that identify neurodegenerative risk either through cause of death or clinical diagnoses. To address the aim of this systematic review, the following two objectives were explored:

1) To explore the presence and direction of a relationship between high impact contact sports participation and young-onset dementia.

2) To explore whether there are differences in relationships across individual high-impact contact sports.

## 2. Methods

### *2.1 Search Strategy*

The protocol of this systematic review was registered with PROSPERO [ID: CRD42023423143], the review is reported in accordance with the PRISMA guidelines A [27] (see Supplement file 1: Appendix 6 for checklist). To align with a systematic review of aetiology, the review question, search terms, and inclusion/exclusion criteria were structured around a Participant, Exposure, Outcome (PEO) framework [28].

The search strategy was conducted by the lead researcher (TF) in consultation with an information specialist at University of Liverpool. Five databases were searched from date of inception until April 2024 (Web of Science, Medline (Ovid), APA Psychinfo, CINAHL, and SportsDiscus), to keep the search results updated, this was repeated regularly until November 2025. The search string consisted of three domains regarding type of contact sports, terms relating to head injury, and forms of clinically diagnosable dementia, with Mesh terms and some search terms customised for each database. The search strategy was designed to be expansive, including a variety of different terms relating to repetitive head injury and various forms of dementia. Determination of contact sports was informed by previous systematic reviews linking sports to concussion incidence, including different forms of individual and team sports [29,30]. As a result, some sports not always considered contact sports were included if there has been evidence of an association of head injuries, such as cycling [22], and equestrian-related sports [67]. A list of combat sports was also included due to suggestions that concussion incidence may differ across them [31,32] (See Supplement file 1: Appendix 2 for full search strategy). Searches were restricted to articles published in English and there were no restrictions on publication date. Theses, books, and conference abstracts were excluded. Search results were transferred to the online programme CADIMA [33], removal of duplicates was completed using this tool, and then manually by the lead researcher.

### *2.2. Study eligibility*

Studies were eligible for inclusion if they were a) original observational research e.g. cross-sectional, cohort, and case-control studies, b) assessed participants associated with contact sports (see search strategy for definition of this), c) evaluated relative risk or data that could be converted into relative risk. Odds ratios were also included, they are not equivalent to relative risk measures but can be used interchangeably to represent risk for low event rates [34].

Studies were also eligible for inclusion if they had samples representing participants who were either under sixty-five years of age, or who were diagnosed with dementia before sixty-five years. Given the anticipated limited number of studies in this field, a broader inclusion approach was adopted, thus studies in which the samples had a mean age of <65 were also included. Studies that reported only the mean age and which did not explicitly focus on 'young-onset dementia' were treated as a separate group and discussed in relation to validating and comparing to the main findings of the included studies. Neurological studies, which often demonstrate dementia-related pathologies, could not be included in the study as they do not report on age at diagnosis. Table 1 shows a full account of the inclusion and exclusion criteria is provided supplement file 1: Appendix 1.

### *2.3 Study selection*

Following the removal of duplicates, three researchers (TF, MP, and AG) independently completed title and abstract screening (stage 1) and full-text screening (stage 2). Any disagreements were discussed with third reviewers (CG/CS). The PRISMA flowchart of inclusion and exclusion of studies for this review is provided in Figure 1, further details relating to reasons for exclusion during the stage 2 process are provided in supplement file 1: Appendix 4.

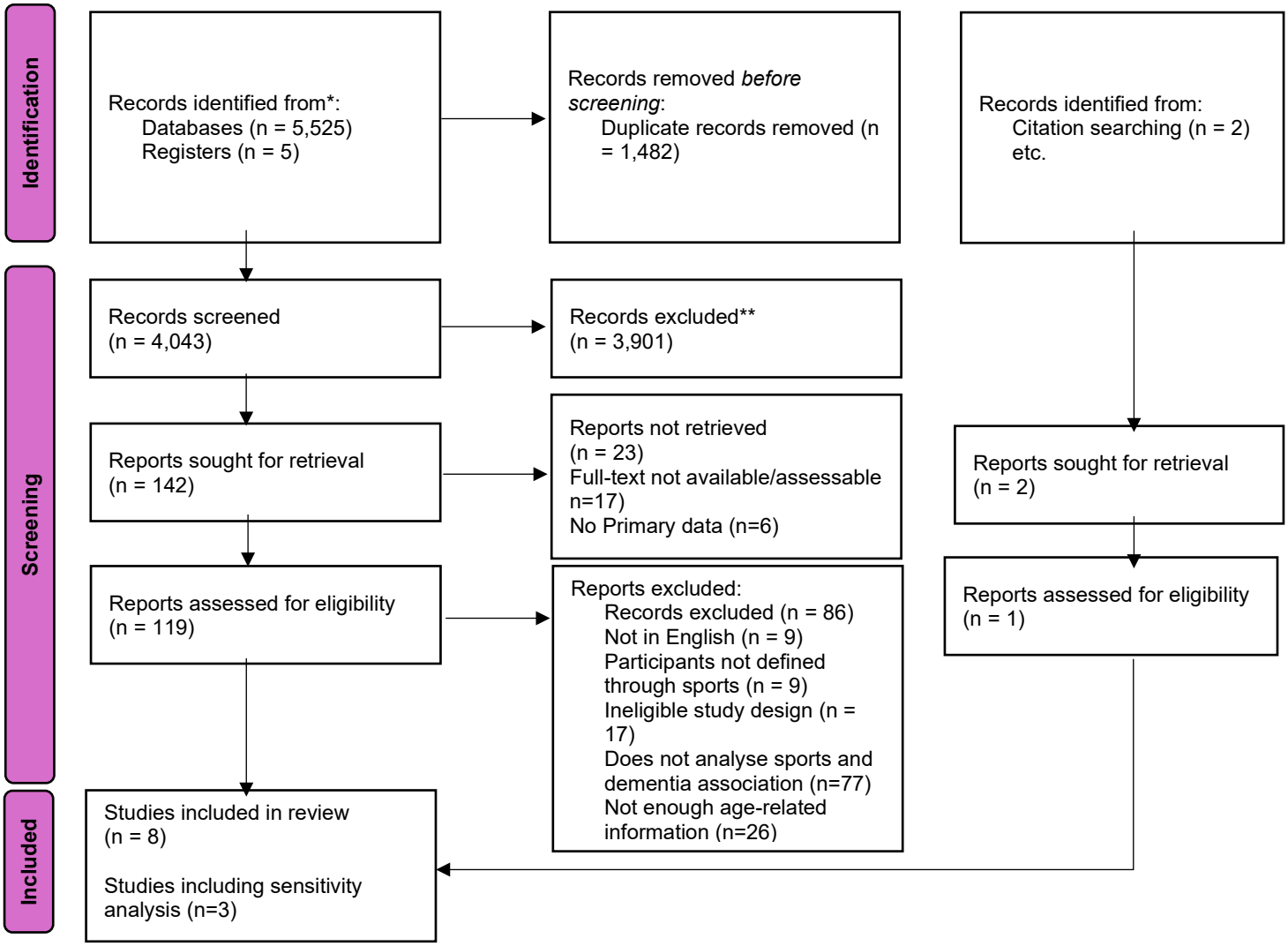


**Figure 1: Flowchart of study selection, adapted from the PRISMA 2020 statement**

*2.4 Data Extraction*

Data were extracted after extensive review of each publication; this was conducted independently by two researchers (TF and MP) into Microsoft Excel. Disagreement was resolved by discussion, if consensus was not achieved arbitration was undertaken by a third reviewers (CG/CS). Extracted data included participant characteristics, reported nature and amounts of head injury, how head injuries were reported (self-report, questionnaire etc.), type of sports, amateur/(semi) professional, type of diagnosis and how it was determined (medical records, self-reported etc.), additional variables included study design, information on control groups, alternative variables measured, study characteristics (country, year), and the study conclusions.

*2.5 Assessment of methodological quality*

Methodological quality and risk of bias was assessed using the Newcastle-Ottawa Scale tool for non-randomised observational studies, with scales for cross-sectional, cohort, and case-control studies [35]. With this tool, quality and bias is assessed in three categories, the comparability of groups, the selection of study groups, and the ascertainment of either exposure (case-control) or outcome of interest (cohort study and cross-sectional studies). Studies are scored out of a possible nine points, where more points denote a lower risk of bias and higher methodological quality, this is then labelled as either unsatisfactory (<4), fair (5-7), or good (>8). As the tool was originally designed for cohort and case-control studies, assessment for cross-sectional studies was conducted using a modified version of the Newcastle-Ottawa scale for the current study (see Supplement file 1: Appendix 3). Quality assessment was utilised to inform on the variability of study quality across the selected studies and was not used as a basis on whether to include or exclude studies. Two reviewers (TF and MP) completed the quality assessment independently, and any disagreements were resolved through discussion.*2.6*

*Methods of Synthesis*

A narrative synthesis was adopted due to methodological and statistical heterogeneity across the included studies. A meta-analysis was not appropriate due to variation in unit measurements, age boundaries of early onset dementia, and comparators used within the studies. Firstly, out of the five studies which reported direct evidence on the event rates of early onset dementia, only three studies had a standardised unit that was similar across individual studies, and the remaining studies could not be converted to similar unit measurements using any method. Of the three studies which had prevalence ratios, they all used different time periods for the onset of dementia. Furthermore, two studies used the same dataset, which would breach the rule of independence, as we would be double counting the same dataset twice. The remaining studies were even more varied, which made comparison or meta-analysis inappropriate. Studies were therefore analysed based on the direction of association. Measures of risk were recorded as presented in the study (hazard ratios, odds ratios, standard mortality ratios) or initially recorded and subsequently converted into prevalence ratios (prevalence point estimates, percentage scores), this was done manually, and statistical tests were not required for this process. Risk estimates were presented alongside 95% confidence intervals and p values.

*Amendments to protocol*

Throughout the conceptualisation and design stages of the review, some minor amendments were made which deviated from the original design in the protocol. These were mostly changes relating to expanding the search strategy to provide a more extensive account of high impact contact sports. For example, the protocol originally stated boxing, wrestling, and martial arts, but it was decided to expand this to include the term "combat sports" and a range of individual forms of martial arts. Hockey was also expanded to include both field and ice-hockey, and equestrian was expanded to include horse-racing as this was more reflective of research associating equestrian-related sport to concussion risk [67]. The original protocol also included seven databases, one database was removed due to becoming defunct, while another database, Scopus, was not included as this has significant overlap with the other included databases.

*2.7 Subgroup analysis*

Subgroup analyses were conducted based on the commonality of sports. Studies in which the participants participated in the same sports will be compared to assess the associations within each sport.

*2.8 Sensitivity analysis*

A sensitivity analysis was conducted to assess the inclusion or exclusion of studies where age-stratified groups partially included individuals over 65.

## 3. Results

Our search strategy identified 5,525 initial records with 1,482 duplicated records manually removed. A total of 4,043 abstracts were screened (stage 1) and from these 119 records were included in the full-text screening (stage 2). After screening, eight studies were included in the main analysis of the review. This data are presented in a custom format in Table 1.

**Table 1: Summary of included studies.**

| Group 1 Studies: Direct Comparisons to young-onset dementia | | | | | | | | | | | |
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| | | Exposure | | Outcome | | Population | | | Summary of Findings | | |
| **Author (country, year of publication), study design** | **Sport (amateur vs professional)** | **Mean Career Length in years (SD)** | **Head Injury / Concussions** | **Dementia Type** | **Source of Diagnosis** | **N. cases of exposure/total cases** | **Comparison Group** | **Age Related Information** | **OR's/ HR's (95% CI) or PR/SMR/PPE/%.** | **Quality/Risk of Bias** | **Comments** |
| **Adani (2020, Italy), Case-Control** | Association Football, Athletics, Volleyball, cycling. | Not measured. | Not measured. | Alzheimer's (AD) (n=32) and Fronto-Temporal Dementia spectrum (FTD) (n=19) | Self-Report | Exposure Groups n/total n<br><br>Competitive Sport Dementia: 4/54<br><br>Competitive Sport AD: 1/31<br><br>Competitve Sport FTD: 3/16<br><br>Football Dementia: 7/51<br><br>Football AD: 3/29<br><br>Football FTD: 3/16<br><br>Cycling Dementia: 5/53 | Control Group n/total n –<br><br>Competitve Sport Dementia: 8/46<br><br>Competitive Sport AD: 8/46<br><br>Competitive Sport FTD: 8/46<br><br>Football Dementia: 4/50<br><br>Football AD: 4/50 | Average age of disease onset – 59.3 (4.7) | Soccer OR:<br><br>Dementia 2.23 (0.54-9.26)<br><br>Alzheimers: 1.78 (0.32-10.08)<br><br>Fronto Temporal Dementia: 2.62 (0.43-15.90)<br><br>Cycling OR's:<br><br>Dementia 2.28 (0.39-13.43)<br><br>Alzheimer's: 0.60 (0.07 – 6.20) | ********** **(Fair)** | Study reports that football increases the odds of Alzheimer's Disease and Fronto-Temporal. Cycling increases odds of fronto-temporal dementia but not football. However wide confidence intervals for all results with no statistical significance.<br><br>Volleyball, swimmi |

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| | | | | | | Cycling AD: 1/31<br><br>Cycling FTD: 3/16. | Football FTD: 4/50<br><br>Cycling Dementia: 2/52<br><br>Cycling AD: 2/52<br><br>Cycling FTD: 2/52 | | Frontotemporal: 4.37 (0.62-30.93) | | ng, running, sport in general, and playing competitive sport decreased the odds of dementia significantly |
| **Lempke (2023, USA), Cross-Sectional** | NFL (Professional and amateur) | 17.5 - median 5 as professional | Not Measured. | Any Dementia | Self-Report | Ages – n/total n<br><br>Total participants: 1784<br><br>30-39 – 6/360<br>40-49 – 8/285<br>50-59 – 19/321<br>60-69 – 35/360 | Hendricks et al (2021) samples from "High Income Economies"–<br><br>40-49 – 32.3/100,000<br><br>50-59 – 115.2/100,000 | Stratified in nines. | **PR's:**<br><br>40-49 – 10.42 (4.32 – 24.87), p<0.0001<br><br>50-59 – 9.24 (5.7 - 14.98), p < 0.001 | ******** **(Fair)** | Players are self-reporting dementia as young as 30-39. Comparison can be made from two age bands, showing much higher prevalence in NFL samples compared to general population. |
| **Willer (2018, UK), case-control** | NFL + Ice-Hockey (NHL) (Professional) | 8.5 – minimum 2 seasons. | Retrospective discussions - but data eliminated due to lack of reliability. | Early-onset dementia. | Through cognitive and clinical assessment. | 0/21 | 21 ice-hockey group. | All participants <65 years. | None of the participants could be diagnosed with early-onset dementia. | ****** (Fair) | None of the participants met the criteria for dementia. |

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| **Walton (2022, USA), Cross-Sectional** | NFL (Professional) | 17.7 (4.7) | Self-reported concussion histories provided and showed positive associated with dementia. | Alzheimer's, fronto-temporal, lewy-body, other dementias. | Self-Report | n/total n: 82/922<br><br>50-54: 9/128<br><br>55-59: 8/179<br><br>60-64: 13/166 | High-Income Country Prevalence from Hendricks et al (2021):<br><br>50-54 – 81.3/100,000<br>55-59 – 148.5/100,000<br>60-64 – 663.9/100,000 | Ages of exposure group stratified into bands of 4 years | PR's using Hendricks (2021):<br><br>50-54: 12 (6.05 – 23.8), p < 0.001<br><br>55-59: 5.84 (2.88 – 11.86), p < 0.001<br><br>60-64: 2.124 (1.232 – 3.66), p < 0.001 | **** (Fair) | Prevalence ratios showed increased risk of dementia for NFL players. Risk increased as ages decreased.<br><br>This study provided a control sample for >65 years, the youngest age group from the Langa et al (2012) control sample showed lower prevalence estimates than all prevalences of the younger age bands (<64) in the study sample. |
| **Weir (2009, USA), cros** | NFL (Professional) | 7.6 – Minimum 3 seasons. | N/A | Alzheimer's/Dementia | Self-Report | Total n =1063<br><br>Events/ Observations: | General Population control | Stratified ages, two groups | 30-49:<br><br>PR: 19 (5.03 – 27), p<0.0001 | **** (Unsatisfactory) | Shows higher rates of dementia at younger ages in |

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| **s-sectional** | | | | | | 30-49 n=7/374<br><br>50+ n=41/670<br><br>30-49 – 1.9%<br><br>50+ 6.1% | 30-49 – 1/1000<br><br>50+ 12/1000 | used in dementia analysis: 30-49 and 50+ | 50+ PR: 5.08 (1.97-8) | | NFL players compared to controls. However, 50+ contains older adult data as well. |

Group 2: Studies with age-related conclusions or with average ages below 65, but without age-specific data.

| **Exposure** | | | | **Outcome** | | **Population** | | | **Summary of Findings** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Author (Year, country), study design** | **Sport (Amateur/Professional)** | **Mean career length (SD)** | **Concussion/ Head injury info.** | **Dementia type.** | **Nature of recording.** | **Exposure group cases of exposure/total cases** | **Comparison cases of exposure/ total cases** | **Age Related Info.** | **Age-adjusted OR's/ HR's (95% CI) or PR/SMR/PPE/% - Significant results in bold.** | **Quality/Risk of Bias** | **Comments** |
| **Guskewitz (2005, USA), Cross-Sectional** | NFL (Professional) | 6.6 (SD 3.6) | 817 reported loss of consciousness; 787 reported memory loss from a historic concussion. | Alzheimer's Dementia. | Self-Report | 33/2552 | Data from general population sample (Brookmeyer et al, 1998) | Mean age 53.8 (+-13.4). | PR: 1.37(.98-1.56) (graph shows larger disparity for <69 years shown graphically but data not reported) | **** (Fair) | Suggests disparity of AD diagnosis to general population is higher at younger ages. But non-significant results and low numbers of dementia. Only >50 years included. |

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| **MacNab (2019, UK), cross-sectional.** | Association Football | N/A | Self-reported concussion 53% of respondents. | Neurodegeneration/ Alzheimer's Disease | Self-Report and clinical telephone assessment. | Soccer Players<br><br>13/468 | General Population Controls<br><br>2/619 | Soccer Players m. age 63.7<br><br>General Population Controls m. age 68.4 | Neurodegenerative disease OR: 3.46(1.25-9.63), p<.002<br><br>Converted RR: 8.4 (1.90 – 37), p < 0.001 | ******** (Good) | Shows younger cohort of soccer players had higher levels of neurodegeneration but did not report relative risk for dementia/Alzheimer's due to only two cases in control sample. |
| **Nguyen (2019, USA), cohort.** | NFL (Professional) | N/A | N/A | Dementia/Alzheimer's Disease | Cause of death from death registers – Dementia either as underlying cause of death, or as a contributor (dying with dem | NFL group dementia as a contributing factor in death registers.<br><br>Contributing factor 16/517 | Baseball Control Group dementia as a contributing factor in death registers<br><br>Contributing factor 10/431 | NFL group average age at death 59.6 (13.2)<br><br>Baseball Control Group average age at death 66.7 (12.3): | Dementia HR: 2.26(0.99-5.17) | ******** (Good) | Positive association for dementia as underlying cause of death, positive association for dementia as contributing factor, non-significant possibly due to low numbers. |

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**OR = Odds Ratios; HR= Hazard Ratios; PPE = Prevalence Point Estimate; SMR = Standardised Mortality Ratios; PR = Prevalence Ratios**

*3.1 Characteristics of the Included Studies*

Eight studies were included in the main analysis, comprising 7,385 individual participants [36-43]. Studies originated from the USA (n=5), UK (n=2), and Italy (n=1). Only two studies were specifically designed to focus on young-onset dementia [36,38], the other studies focused on dementia but provided data in age-stratified groups (n=3), or through a mean age of under sixty-five (n=3). Only one study included women in their sample [36], other studies either included only male samples (n=3) or made no reference to the gender of their samples (n=3). Despite searching for a wide variety of sporting types, most studies represented American Football (n=6), and Association Football (n=2), one study involved players of American football and hockey (NHL). Dementia was identified through self-report of for most studies (n=6), one study identified dementia through medical and death records (Nguyen et al, 2019), and one study utilised cognitive and clinical assessment [38]. Five studies utilised a cross-sectional design, there was one cohort study, and two employed a case-control design. Studies varied in their use of comparators, either using a general population sample (n=3) or non-contact sports as control groups (n=2). Two studies did not employ a comparison group, a recent systematic review on young-onset dementia prevalence was used for an age-matched comparator for the data of these studies. One study did not provide risk-based measures due to a sample with no participants having dementia [38]

*3.2 Association Between head trauma through sports participation and Young-Onset Dementia*

Five studies [36-40] allowed for direct assessment of the association of playing competitive sport with the development of young-onset dementia (<65). Three studies use comparison groups of individuals who did not take part in sporting activities related to repeated head injuries. Two studies only reported the prevalence ratio of the exposed group with no comparator.

Of these five studies, four reported a positive association between participation in sports and self-reported dementia at ages below 65 [36, 38-40], one study could not make conclusions around risk as they found zero participants met the criteria for young-onset dementia [38]. Three studies determined dementia through self-report and used a cross-sectional design with similar sample sizes (922-1786). When calculations of relative risk were compared to global estimated prevalence of young-onset dementia [2], risk for dementia increased for younger cohorts with statistically significant results. This risk was provided across different age groups, showing the strength of the risk increased with younger ages, but spread of confidence also increased. For example, one study showed that players 40-49 aged were at higher relative risk of living with dementia, [PR: 10.42(4.32 – 24.87), $p<0.001$], compared to those aged 50-59, [PR: 9.24 (5.7 – 14.98), $p<0.001$] [37]. While another study found players aged 50-54 had the highest risk [PR: 12 (6.05 – 23.8), $p < 0.0001$], compared to those aged 55-59, [PR: 5.84 (2.88 – 11.86), $p < 0.001$], and those aged 60-64, [PR: 2.124 (1.232 – 3.66), $p< 0.001$] [39].

Four of these studies did not provide a control group that was appropriate for ages under 65 e.g. Walton et al. (2022) provided a comparison sample only up to 65 years. A recent systematic review that provided young-onset

dementia prevalence in a variety of age-groups was used as a comparison group to elicit relative risk estimates [2]. These estimates indicated an extremely large, statistically significant positive association between young-onset dementia and American Football, however, are based on unbalanced samples and wide confidence intervals. Finally, it was suggested that cycling may be a risk factor for dementia in one case-control study, OR: 2.28 (0.39-13.43), but not Alzheimer's disease [OR: 0.60 (0.07 – 6.20)].

Three studies provided sample populations that could be partially compared to young-onset dementia through a mean exposure sample age at under sixty-five [41-43]. This was determined either through an overall mean sample age of less than 65 years [41], or a mean age of the exposure group under sixty-five [42,43].

Two studies focused on NFL players [41,43]. Attribution of dementia differed between the studies, either through self-reported dementia in a cross-sectional analysis [41] or retrospective cohort identifying diagnosis from death records across NFL and baseball players [43]. Both studies reported a positive association between a career in American Football and dementia, [PR: 1.37(.98-1.56); HR: 2.26(0.99-5.17)]. However, no study provided p values, and the confidence intervals of each relevant effect indicate that none of the associations reached statistical significance in two studies [41,43].

*3.3 Subgroup analysis - Association Football vs American Football*

Six studies focused on American Football [37 – 41, 43], and two studies focused on Association Football [36,42]. Of the NFL studies, five showed a positive association to developing dementia at young ages [37, 39-41, 43]. The two studies focusing on football reported increased odds of having a dementia diagnosis for footballers in their young samples [36,42]. These studies differed in the statistical significance of their results, as Adani et al (2020) reported wide confidence intervals and non-significant associations, while MacNab et al (2019) reported significant results. In terms of the age-related direction of risk, four NFL studies suggested higher relative risk of dementia for younger age samples when compared to comparators or equivalent general population samples [37, 39-41].

*3.4 Sensitivity Analysis*

To assess the extent to which the study findings were influenced by the age-based exclusion criteria, a sensitivity analysis was performed (see supplement file 1: Appendix 5). This analysis included two cohort studies of association football and one of American Football that were excluded from the original analysis as their eligibility relating to age could not be completely determined [44-46]. All three studies ascertained dementia through hospital and death records, two stratified groups based on participants birth years or years of first season [44,45], and one study provided a median age at death of 54 years and age-stratified data showed a majority of the sample were of younger age, but 9% of the sample was over 70 years at the time of death [46]. Of these studies, two showed positive associations between participation in association football and dementia [44,46], supporting the findings of the main analysis. However, one study did show a conflicting result as their youngest age-group were also the only group in their study that did not show a positive association between association football and dementia [45].

*3.5 Methodological Quality*

Quality assessment for the included studies is presented in table 1. Studies scored between 4 and 8 stars. Two studies scored eight stars [42,43], indicating good quality, and five studies were scored between five and seven stars, indicating fair quality (36-38, 41, 42]. On selection criteria, reasons for losing stars related to sample sizes that were not appropriate or designed for a low prevalence population like young-onset dementia [36,38], and three cross-sectional studies also had unsatisfactory drop-out rates [40-42]. In four cross-sectional studies statistical tests were not fully reported and for six studies the assessment of their outcomes (diagnosis of dementia) relied on self-report in questionnaires (36, 37, 39-42].

## 4. Discussion

This systematic review is the first to explore the association of sports participation and young-onset dementia. Eight studies were included in the review; studies were of varying quality ranging from unsatisfactory to good and there was substantial variation in methodology and the presentation of age-related data. The review is supportive of previous reports identifying traumatic brain injury as an important consideration in the development of dementia at younger ages [14, 47, 48] and adds to previous reviews suggesting an association between professional sport participation and dementia [49-51].

The review highlights the paucity of research that reports on young onset dementia risk in high contact sports. From the results reported, there may be limited evidence of a larger than expected sample of middle age NFL athletes with dementia compared to a high-income general population. In the included studies, NFL participation was associated with higher levels of dementia at young ages, and this was generally consistent except for one study with a low sample size. These associations were more likely to show statistical significance in studies that provided direct age comparisons. Additionally, the direction of these findings was consistent across different methodologies, there was statistically significant higher risk compared to high economy population samples [2.124 (1.232 – 3.66), $p < 0.001$]. Where age groups were stratified, younger age groups showed higher levels of risk, but confidence intervals were also increased because of smaller samples. Higher risk was also reported when compared to non-contact control group (HR: 2.26), and general population samples (PR: 1.37). However, caution should be applied to these results due to wide confidence intervals from small sample sizes.

American Football has been shown to expose players to repetitive concussive [52] and sub-concussive [20] impacts, and the findings support previous concerns on adverse neurological consequences that may be associated with these [53-55]. Controversy remains on whether such links should be considered alongside additional risk factors for dementia, including genetics [56], and adverse childhood experiences [57]. However, with physical health risk factors, there is growing evidence that athletes may have lower risk of exposure, suggesting that brain health is more likely to be a contributing factor to the increased risk shown in this study [49]. The relative contribution of these factors in athlete populations for those under 65 remains unclear, and future research should aim to disentangle these effects through longitudinal and multivariable analyses.

The evidence for association football (soccer) is more limited but points in a similar direction. The included studies suggest that increased dementia risk may also be present in younger age groups of former players [36,42]. With only two studies available to assess, any conclusions made are cautious, however further studies were considered in a sensitivity analysis which found similar trends, with one exception [45]. This is broadly consistent with previous research linking repetitive heading and head collisions in Association football to potential long-term

neurological effects, although the magnitude and mechanisms of risk may differ from those observed in American football due to variations in impact frequency and intensity. Focused evidence of young-onset dementia in soccer players is largely limited to case studies [58], so it is important that the findings of this review are further explored in high quality observational research that considers risk across different age groups.

## 5. Limitations and recommendations

While a strict eligibility criterion added rigour to the review, many studies were excluded due to low confidence in their representation of young-onset dementia. As young-onset dementia is a rare condition, with prevalence little over 0.1% [2] this compels observational studies of dementia to omit <64 age groups, therefore many large-scale cohort studies measuring dementia in athletes were excluded. Of the included studies, only two studies were measured as "good" quality, and some cross-sectional studies relied on participants self-reporting dementia, which may not accurately portray dementia rates. Despite a wide range of sports included in the search strategy, eligible studies only represented American Football and soccer. The focus on clinically diagnosable young-onset dementia may have led to the exclusion of some relevant studies, particularly neurological studies where age of diagnosis cannot be discerned.

The lack of literature on boxing is perhaps surprising given the history of case-studies showing progressive neurodegeneration in ex-boxers [59,60], and research associating an earlier onset of Alzheimer's disease to boxing [61]. Research has shown that concussion risk exists across a variety of different sports, including rugby [63] and combat sports [64], leading to increasing concerns around early-onset dementia in Rugby Union in recent years [62]. Evidence so far appears to suggest low risk of dementia in former rugby players, however the available evidence could either not be attributed to young onset dementia [65] or did not report adequate control data to determine relative risk [66]. The included studies also suffered from low representation of female athletes, highlighting a wider concern in sports within dementia literature. For future research to accurately portray the long-term impact of sports participation and concussions, it would be useful to explore a wider range of sports and greater representation of populations.

## 6. Conclusions

Young-onset dementia remains an uncommonly diagnosed condition, and this is still the case for athletes. Despite this, there is some limited evidence that athletes of sports associated with exposure to concussions may have a higher risk of developing young-onset dementia compared to the general population or control samples. The review suggests limited evidence that NFL players may have increased risk of dementia at younger ages, with some consistency in the direction of this risk across varying methodologies. Risk may differ across different sports; however, this review was only able to assess two sports. The review suggests limited evidence of increased risk of young-onset dementia in soccer players when a sensitivity analysis was conducted, although this wasn't entirely consistent. The results should be interpreted with caution due to challenges associated with assessing a low prevalence population; confidence intervals tended to be extremely wide, and p values were not always reported. Studies were generally of moderate quality and there was a low amount of cohort studies due to the age-related exclusion criteria; studies were not always reflective of young-onset dementia, as they did not specifically focus on young ages, so only studies with stratified age-groups or mean ages <65 could be considered. The review

highlights the dearth of representation of young-onset dementia in the sporting literature and recommends future studies place more emphasis on this area.

## Statements and Declarations

### Conflicts of Interest

There are no conflicts of interest to declare from any of the members of the research team. All authors confirm that they have read the Springer "Competing Interests" policy and have no conflicts to declare relating to funding, employment, financial interests or non-financial interests.

## 7. Declarations

### Consent for Publication

Not applicable

### Availability of Data and Materials

Data sharing was not applicable for this manuscript as no datasets were generated or analysed.

### Ethics approval and consent for participate

Not applicable.

### Competing Interests

The authors declare they have no competing interests.


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### Authors Contributions

TF was the lead author of this manuscript, and was responsible for designing, conceptualising, analysing the results, and writing the report. CG and CS were supervisors of the lead author. JH is a statistician and offered expert support in interpreting and assessing the studies. MP and AG were second and third reviewers, supporting in the screening of abstracts and full-texts, and quality appraisal.

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**Supplementary documents:**

**Appendix 1**

**Table 1: Inclusion/Exclusion criteria:**

| **Participant, Exposure, Outcome (PEO)** | **Inclusion Criteria** | **Exclusion Criteria** |
|---|---|---|
| **Participant** | Age of sample representative of young-onset dementia, either through specific age details inc**,** age-stratified groups, or mean sample age <65 years. | Older Adults (>65years), and children (<18 years) |
| **Exposure (Sport)** | Participants must be associated with a sporting vocation considered as high-impact or previously identified through risk of concussions. | Athletic vocations not associated with riskof concussions e.g. swimming, running. |
| **Outcome (Dementia)** | Dementia identified either through evidence of clinically diagnosable dementia (medical registers or death records), detailed examination leading to conclusion of dementia, or through self-reporting. | Neurodegenerative diseases that are not clinically diagnosable and dementia is not mentioned e.g. chronic traumatic encephalopathy.<br><br>Idiopathic neurodegenerative diseases where dementia is not |

| | | |
|---|---|---|
| | | identified e.g. Parkinson's, Korsakoff's, Amyotrophic Lateral Sclerosis. |
| | Observational Non-randomised Studies (prospective cohort, retrospective cohort, cross-sectional, case-control etc.) | Non-observational studies and case-studies. |
| | Contain relative risk scores or data that can be converted into risk scores e.g. HR's, OR's, PR's etc. | |
| **Outcome (Dementia)** | Dementia as a secondary diagnosis to other diseases, if mentioned e.g. Parkinsons with dementia, Chronic Traumatic Encephalopathy with dementia. | |
| **Outcome (Dementia)** | | Studies assessing long-term cognitive change but not mentioning dementia.<br><br>Neuropathologic studies |

**Appendix 2:**

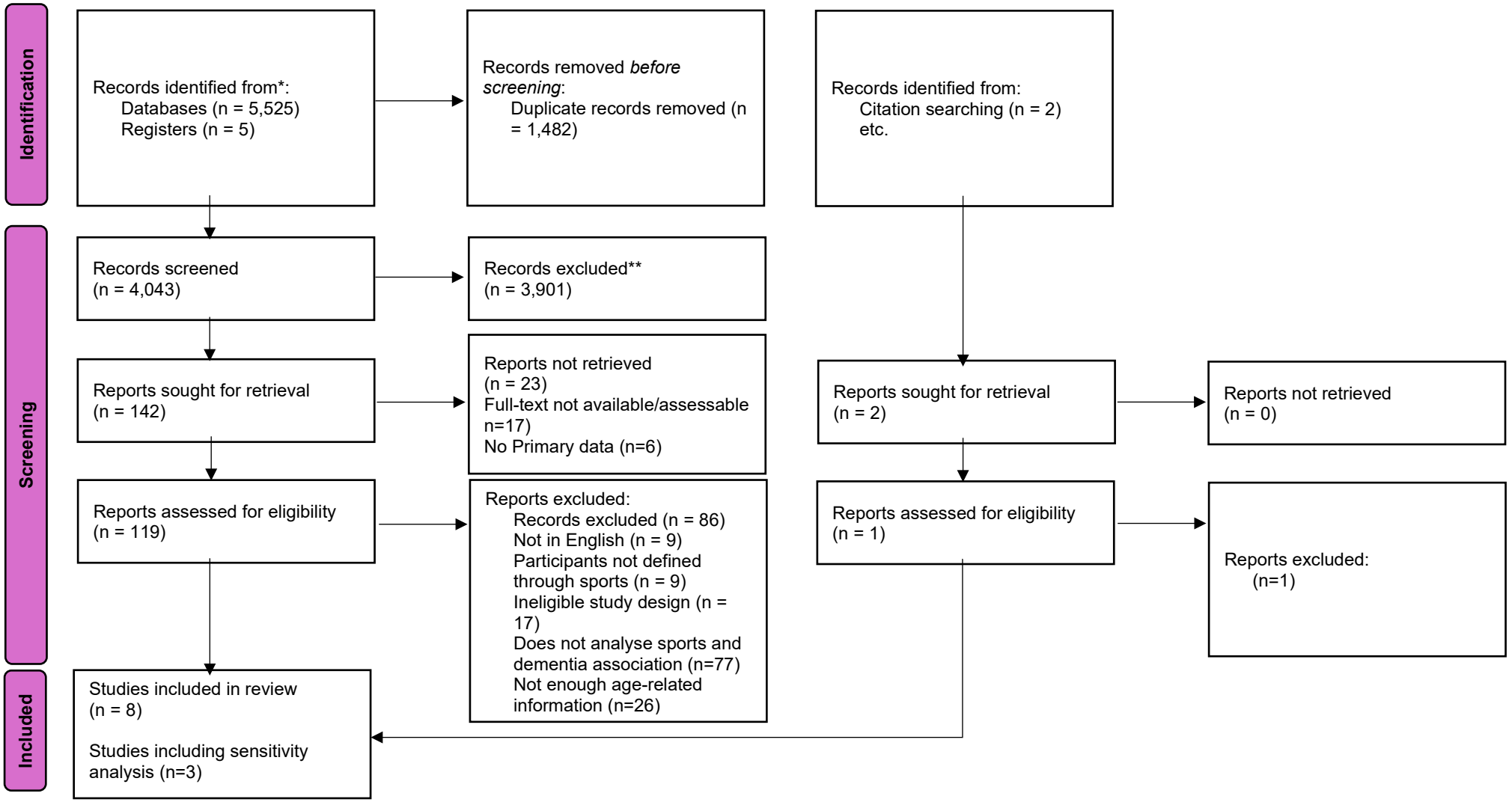


**Figure 1: Flowchart of study selection, adapted from the PRISMA 2020 statement**

**Appendix 3: Search Strategy**

| Database Source | Search String |
|---|---|
| Web of Science | DE "Boxing" OR DE "Sports" OR DE "Athletes" OR DE "Athletic Participation" OR DE "Basketball" OR DE "College Sports" OR DE "Cycling" OR DE "Extreme Sports" OR DE "Football" OR DE "High School Sports" OR DE "Judo" OR DE "Martial Arts" OR DE "Professional Sports" OR DE "Soccer" OR DE "Athletic Injuries" OR horse-riding or equestrian or gymnastics or snow sports or lacrosse or nfl or national football league or american football or australian rules football or gaelic or rugby or "tackle sports" or amateur or biker* or cyclist* or boxer* or fighter* or footballer* or gymnast* or jockey* or horse*rider* or judoka* or wrestler* or aikido or judo or ju-jitsu or muay-thai or taekwondo or karate or kickbox or tai ji or jiujitsu or mixed martial art* or dim mak or kenbo or kung fu or ufc or ultimate fighting championship or boxing in a booth or bare knuckle or white collar or pitfight or submission fight or varsity or gridiron or goalie or goalkeeper or defender or midfielder or forward or "half-back" or "centre-back" or "full-back" or quarterback or "line back" or southpaw or "fly half" or "scrum half" or flanker or slugger or brawler AND DE "Dementia" OR DE "Alzheimer's Disease" OR DE "Dementia with Lewy Bodies" OR DE "Frontotemporal Lobar Degeneration" OR DE "Senile Dementia" OR DE "Vascular Dementia" OR DE "Corticobasal Degeneration" OR DE "Picks Disease" or "earl* onset" or "young* onset" or posterior cortical atrophy or tdp-43 or progressive supra-nuclear palsy or dementia pugilistica or proteinopath* or tauopath* or "neurodegenerative diseases" or "chronic traumatic encephalopathy" or cte AND DE "Brain Concussion" OR DE "Post-Concussive Symptoms" or- head injury or concuss* or sub-concuss* or subconcuss* or traumatic brain injur* or tbi or craniocerebral adj 2 trauma* or impact* or injur* or repetitive or multiple or cumulative adj 3 head injur* or head impact or head trauma or mild head adj 2 injur* or trauma or impact or mtbi |
| Medline (ovid) | 3 young onset.mp. 1918 4 early onset.mp. 47375 5 exp athletic injuries/ or exp athletics/ 233603 6 exp sports/ or exp basketball/ or exp bicycling/ or exp boxing/ or exp football/ or exp hockey/ or exp martial arts/ or exp tai ji/ or exp rugby/ or exp soccer/ or exp team sports/ or exp volleyball/ or exp wrestling/ or exp youth sports/ 217186 7 (horse-riding* or horse-racing* or equestrian* or gymnastics* or snow sports* or lacrosse* or nfl* or american football* or australian rules football* or gaelic).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 11287 8 (biker* or cyclist* or boxer* or fighter* or footballer* or gymnast* or jockey* or horse*rider* or judoka* or wrestler*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 17447 9 (aikido or judo or ju-jitsu or muay-thai or taekwondo or karate or kickbox or tai ji or jiujitsu or mixed martial art* or dim mak or kenbo or kung fu or ufc or ultimate fighting championship or boxing in a booth or bare knuckle or white collar or pitfight or submission fight).mp. |

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| | [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 6959 10 (professional or amateur or varsity or gridiron or college or goalie or goalkeeper or defender or midfielder or forward or half-back or centre-back or full-back or quarterback or line back or guard or southpaw or wing or fly half or scrum half or flanker or hooker or scrum or slugger or brawler).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 669681 11 5 or 6 or 7 or 8 or 9 or 10 899446 12 exp brain injuries, traumatic/ or exp brain concussion/ or exp brain injury, chronic/ 25805 13 exp contrecoup injury/ or exp post-concussion syndrome/ 1642 14 exp Craniocerebral Trauma/ 179199 15 (concussion or concussed or concussive or sub-concuss* or subconcuss*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 17112 16 (traumatic brain injur* or tbi).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 54827 17 ((head adj 2 injur*) or trauma* or impact*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 2063421 18 (((repetitive or multiple or cumulative) adj 3 head injur*) or head impact or head trauma or concussion or subconcussive).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 27260 19 (((repetitive or multiple or cumulative) adj 3 head injur*) or head impact or head trauma or concussion or subconcussive).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 27260 20 ((craniocerebral adj2 trauma*) or impact* or injur*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept |

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| | word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 2942878 21 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 3175874 22 exp dementia/ or exp alzheimer disease/ or exp corticobasal degeneration/ or exp primary progressive nonfluent aphasia/ or exp dementia, vascular/ or exp frontotemporal lobar degeneration/ or exp frontotemporal dementia/ or exp lewy body disease/ or exp mixed dementias/ 206219 23 neurodegenerative diseases/ or exp supranuclear palsy, progressive/ or exp tdp-43 proteinopathies/ or exp frontotemporal lobar degeneration/ or exp frontotemporal dementia/ or exp primary progressive nonfluent aphasia/ 55857 24 (posterior cortical atrophy or chronic traumatic encephalopathy or cte).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 5319 25 22 or 23 or 24 254604 26 3 or 4 or 25 299459 27 21 and 26 27551 28 11 and 27 1501 DE "Boxing" OR DE "Sports" OR DE "Athletes" OR DE "Athletic Participation" OR DE "Basketball" OR DE "College Sports" OR DE "Cycling" OR DE "Extreme Sports" OR DE "Football" OR DE "High School Sports" OR DE "Judo" OR DE "Martial Arts" OR DE "Professional Sports" OR DE "Soccer" OR DE "Athletic Injuries" OR horse-riding or equestrian or gymnastics or snow sports or lacrosse or nfl or national football league or american football or australian rules football or gaelic or rugby or "tackle sports" or amateur or biker* or cyclist* or boxer* or fighter* or footballer* or gymnast* or jockey* or horse*rider* or judoka* or wrestler* or aikido or judo or ju-jitsu or muay-thai or taekwondo or karate or kickbox or tai ji or jiujitsu or mixed martial art* or dim mak or kenbo or kung fu or ufc or ultimate fighting championship or boxing in a booth or bare knuckle or white collar or pitfight or submission fight or varsity or gridiron or goalie or goalkeeper or defender or midfielder or forward or "half-back" or "centre-back" or "full-back" or quarterback or "line back" or southpaw or "fly half" or "scrum half" or flanker or slugger or brawler AND DE "Dementia" OR DE "Alzheimer's Disease" OR DE "Dementia with Lewy Bodies" OR DE "Frontotemporal Lobar Degeneration" OR DE "Senile Dementia" OR DE "Vascular Dementia" OR DE "Corticobasal Degeneration" OR DE "Picks Disease" or "earl* onset" or "young* onset" or posterior cortical atrophy or tdp-43 or progressive supra-nuclear palsy or dementia pugilistica or proteinopath* or tauopath* or "neurodegenerative diseases" or "chronic traumatic encephalopathy" or cte AND DE "Brain Concussion" OR DE "Post-Concussive Symptoms" or- head injury or concuss* or sub-concuss* or subconcuss* or traumatic brain injur* or tbi or craniocerebral adj 2 trauma* or impact* or injur* or repetitive or multiple or cumulative adj 3 head injur* or head impact or head trauma or mild head adj 2 injur* or trauma or impact or mtbi |
| APA Psychinfo/CINAHL/SportsDiscus (combined) | (DE "BOXING" OR DE "COLLEGE boxing" OR DE "KNOCKOUTS (Boxing)" OR DE "WOMEN'S boxing" OR DE "BOXING -- History") OR (DE "SPORTS" OR DE "AMATEUR sports" OR DE "COLLEGE sports" OR DE "COMBAT sports" OR DE "CONTACT sports" OR DE "EXTREME sports" OR DE "GAELIC games" OR DE "GYMNASTICS" OR DE "HOCKEY" OR DE "INDIVIDUAL sports" DE "PROFESSIONAL sports" OR DE "TEAM sports" OR DE "WOMEN'S sports") OR DE "CYCLING" OR DE "WOMEN'S cycling" OR DE "CYCLING injuries" OR DE "EQUESTRIANISM" OR DE "DRESSAGE" OR DE "GAMES on |

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| | horseback" OR DE "GYMKHANAS (Equestrianism)" OR DE "HAUTE ecole (Equestrianism)" OR DE "HORSEMEN & horsewomen" OR DE "HUNT riding" OR DE "RIDING clubs" OR DE "FOOTBALL" OR DE "ARENA football" OR DE "CANADIAN football" OR DE "COLLEGE football" OR DE "HIGH school football" OR DE "SOCCER" OR DE "INDOOR soccer" OR DE "WOMEN'S soccer" OR DE "RUGBY football" OR DE "COLLEGE rugby football" OR DE "RUGBY League football" OR DE "RUGBY Union football" OR DE "RUGBY competitions" OR DE "RUGBY football for children" OR DE "RUGBY football for girls" OR DE "SEVEN-a-side rugby football" OR DE "UNIVERSAL football" OR DE "WOMEN'S rugby football" OR DE "HOCKEY" OR DE "BANDY (Winter sport)" OR DE "COLLEGE hockey" OR DE "FIELD hockey" OR DE "HOCKEY competitions" OR DE "HOCKEY for girls" OR DE "INDOOR hockey" OR DE "LAWN hockey" OR DE "MINOR league hockey" OR DE "RINGETTE (Game)" OR DE "ROLLER hockey" OR DE "TABLETOP hockey (Game)" OR DE "WOMEN'S hockey" OR (DE "MARTIAL arts" OR DE "BUDO" OR DE "EAST Asian martial arts" OR DE "ESCRIMA" OR DE "JEET Kune Do" OR DE "JU-kenpo" OR DE "KAJUKENBO" OR DE "KALARIPPAYATTU" OR DE "KENJUTSU" OR DE "KENPO" OR DE "KICKBOXING" OR DE "KRAV maga" OR DE "KUN-tao" OR DE "LION dance" OR DE "MIXED martial arts" OR DE "NINJUTSU" OR DE "PENCAK silat" OR DE "SAN-jitsu" OR DE "SPEAR fighting") or "horse-racing" or equestrian or gymnastics or "snow sports" or lacrosse or nfl or "national football league" or "american football" or "australian rules" or "tackle sports" or amateur or biker* or cyclist* or boxer* or fighter* or footballer* or gymnast* or jockey* or horse*rider* or judoka* or wrestler* or aikido or judo or ju-jitsu or muay-thai or taekwondo or karate or kickbox or jiujitsu or kenbo or "kung fu" or ufc or "ultimate fighting championship" or "boxing in a booth" or "bare knuckle" or "white collar" or pitfight or "submission fight" or varsity or gridiron or goalkeeper or defender or midfielder or forward or "half-back" or "centre-back" or "full-back" or quarterback or "line back" or southpaw or "fly half" or "scrum half" or flanker or slugger or brawler AND DE "BRAIN concussion" OR DE "POSTCONCUSSION syndrome" OR DE "BRAIN diseases" OR DE "BRAIN injuries" OR mild brain injur* or contrecoup injur* or craniocerebral trauma or concussion or concuss* or sub-concuss* or subconcuss* or tbi or head adj 2 injur or trauma* or impact* or repetitive or multiple of cumulative adj 3 head injur* or head impact or head trauma or craniocerebral adj 2 trauma* or impact* or injur* AND (MH "Frontotemporal Dementia+/EP/ET/PA/PC/RF") OR (MH "Dementia, Senile+") OR (MH "Lewy Body Disease") OR (MH "Mixed Dementias/EP/PA/PC/RF") OR (MH "Frontotemporal Lobar Degeneration+/RF/PA/ET/EP") OR (MH "Dementia+/EP/PA/RF/ET") OR (MH "Dementia, Vascular+") OR (MH "Supranuclear Palsy, Progressive") OR (MH "Alzheimer's Disease/EP/PA/RF") OR (MH "Chronic Traumatic Encephalopathy") OR posterior cortical atrophy or tdp-43 or progressive supra-nuclear palsy or dementia pugilistica or proteinopath* or tauopath* or neurodegenerative diseases or picks disease or young*-onset or earl*-onset or DE "Dementia" OR DE "Alzheimer's Disease" OR DE "Dementia with Lewy Bodies" OR DE "Frontotemporal Lobar Degeneration" OR DE "Senile Dementia" OR DE "Vascular Dementia" OR DE "Chronic Traumatic Encephalopathy" |

## Appendix 4: Adapted Scale for Cross-Sectional Studies

Newcastle-Ottawa Scale for Methodological Quality for Cross-Sectional Studies – Adapted

1. **Selection (6 stars)**

    a. Representativeness of the sample
        i. Truly representative of sporting participation e.g. participation of high impact e.g. football, rugby, combat sports (boxing, wrestling, hockey etc.) (purposive sampling) **
        ii. Somewhat representative of sporting participation (convenience sampling) *
        iii. No details on sampling
    b. Is the sample size appropriate and justified?
        i. Based on $((z^2. p(1-p))/d^2$ - confidence interval (z) of 1.96, expected prevalence (p) of .113 from Hendricks et al (2021), and precision estimate (d) 0.001. This gives an appropriate sample size of 3,850.
            1. > 3,850 *
            2. < 3,850
    c. Non-response rate
        i. Comparability between respondents and non-respondents' characteristics is established, and the response rate is satisfactory (>75%). *
        ii. The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.
        iii. No description of the response rate or the characteristics of the responders and the non-responders.
    d. Ascertainment of nature (level, frequency) of exposure. How has participation/ number of seasons/ experience head injuries in sports been determined?
        i. Official records of sporting participation or medical records **
        ii. Structured interview/questionnaire *
        iii. Not mentioned

2. **Comparability (1 star)**

    a. The study controls for important confounders (alcohol use, head injuries, smoking) *
    b. The study does not consider or assess for confounders

3. **Outcome (3 stars)**

    a. Assessment of Outcome – Diagnosis of dementia
        i. Hospital/Medical records **
        ii. Structured interview/questionnaire*
        iii. No description/non-standard methods used
    b. Statistical Test
        i. Clearly described, appropriate, confidence intervals and p values included *
        ii. None of above described

**Appendix 5: Study Screening Decision Table**

| | Title of Article | Inclusion/Reason for Exclusi |
|---|---|---|
| 100 | Short term memory functioning in the detection of alzheimer's disease | Full-text not accessible. |
| 185 | Neurological Deterioration in American Football Players | Study does not assess for clini |
| 194 | Developing methods to detect and diagnose chronic traumatic encephalopathy during life: rationale, design, and methodology for the DIAGNOSE CTE Research Project | Study does not assess sport ar<br><br>(A study rationale, not a compl |
| 203 | Cerebral and cognitive modifications in retired professional soccer players: TC-FOOT protocol, a transverse analytical study | Study does not assess for spor<br><br>(Study protocol) |
| 210 | Clinicopathological Evaluation of Chronic Traumatic Encephalopathy in Players of American Football | Not assessing clinically diagno<br><br>(Pathology studies excluded) |
| 219 | Age at First Exposure to Repetitive Head Impacts Is Associated with Smaller Thalamic Volumes in Former Professional American Football Players | Not assessing for sport and clir<br><br>(Pathology studies excluded) |
| 220 | Regional brain atrophy in professional fighters: Different patterns, different mechanisms? | Not original piece of research - |
| 230 | The spectrum of disease in chronic traumatic encephalopathy | Study does not assess for spor<br><br>(Study protocol) |
| 236 | No title | Study not accessible. |
| 243 | 전두측두엽 치매와 파킨슨증의 임상양상을 보이는<br>권투선수치매 1예 | No English version of study ava<br><br>(English abstract) |
| 245 | Dementia Pugilistica with clinical features of Alzheimer's disease | Not an observational study |
| 247 | Cerebrospinal fluid tau, A beta, and sTREM2 in Former National Football League Players: Modeling the relationship between repetitive head impacts, microglial activation, and neurodegeneration | Not assessing for sport and clir |
| 249 | White matter signal abnormalities in former National Football League players. | Not assessing for sport and clir |
| 251 | Long-Term Changes in Brain Connectivity Reflected in Quantitative Electrophysiology of Symptomatic Former National Football League Players | Not assessing for sport and clir |
| 255 | Limbic system structure volumes and associated neurocognitive functioning in former NFL players | Not assessing for sport and clir<br><br>(CTE study) |

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| 257 | Cavum Septi Pellucidi in Symptomatic Former Professional Football Players | Not assessing for sport and cli |
| 261 | Chronic Traumatic Encephalopathy in Athletes: Progressive Tauopathy After Repetitive Head Injury | Not assessing for sport and cli |
| 278 | Incipient chronic traumatic encephalopathy in active American football players: neuropsychological assessment and brain perfusion measures | Not assessing for sport and cli |
| 281 | A quantitative risk assessment for chronic traumatic encephalopathy (CTE) in football: How public health science evaluates evidence | Not an observational study. |
| 282 | Characterizing tau deposition in chronic traumatic encephalopathy (CTE): utility of the McKee CTE staging scheme | Not assessing for sport and cli<br><br>Assesses CTE stage with dem |
| 294 | Professional Fighters Brain Health Study: Rationale and Methods | Not an observational study.<br><br>Rationale of study. |
| 295 | Interactive Effects of Racial Identity and Repetitive Head Impacts on Cognitive Function, Structural MRI-Derived Volumetric Measures, and Cerebrospinal Fluid Tau and A beta | Not assessing for sport and cli |
| 297 | Impact of Playing American Professional Football on Long-Term Brain Function | Not assessing for sport and cli |
| 302 | Proteomic Profiling of Extracellular Vesicles Isolated From Cerebrospinal Fluid of Former National Football League Players at Risk for Chronic Traumatic Encephalopathy | Not assessing for sport and cli |
| 318 | Replication Data for: Mortality Risk Factors among National Football League Players: An Analysis using Player Career and Biometric Data | Not assessing for sport and cli<br><br>Assesses age at death but doe |
| 403 | Age at First Exposure to Tackle Football is Associated with Cortical Thickness in Former Professional American Football Players | Not assessing for sport and cli |
| 406 | Increased Translocator Protein in the Brains of Active and Recently Retired NFL Players: A Pilot Study Using [11C]DPA-713 PET-Based Neuroimaging | Full-text not accessible. |
| 408 | Microglial neuroinflammation contributes to tau accumulation in chronic traumatic encephalopathy | Not assessing for sport and cli |
| 415 | Clinical symptoms of CTE and other neurodegenerative conditions. | Full-text not accessible. |
| 460 | Heading Frequency Is More Strongly Related to Cognitive Performance Than Unintentional Head Impacts in Amateur Soccer Players | Not assessing for sport and cli |

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| 472 | Brain glucose metabolism and gray matter volume in retired professional soccer players: a cross-sectional [F-18]FDG-PET/MRI study | Not assessing for sport and cli |
| 490 | Structural and Functional Brain Changes in Boxers and Mixed Martial Arts Fighters Are Correlated with Fight Exposure | Not assessing for sport and cli |
| 514 | Subjective Concerns Regarding the Effects of Sport-Related Concussion on Long-Term Brain Health among Former NFL Players: An NFL-LONG Study | Not assessing for sport and cli |
| 523 | An Investigation on Repetitive Head Impact Exposure and Plasma Total Tau Concentrations in Former National Football League Players | Full-text not accessible. |
| 524 | Tau Positron Emission Tomography and Neurocognitive Function Among Former Professional American-Style Football Players | Not assessing for sport and cli |
| 528 | Frequency and Predictors of Traumatic Encephalopathy Syndrome in a Prospective Cohort of Retired Professional Athletes | Not assessing for sport and cli |
| 538 | CTE in boxers: modern findings in classic cases | Full-text not accessible. |
| 539 | Mortality Among Professional American-Style Football Players and Professional American Baseball Players | Accepted. |
| 556 | Is There Chronic Brain Damage in Retired NFL Players? Neuroradiology, Neuropsychology, and Neurology Examinations of 45 Retired Players. | Not assessing for sport and cli<br><br>Radiology study, no focus on d |
| 563 | Association of APOE Genotypes and Chronic Traumatic Encephalopathy | Not assessing for sport and cli<br><br>CTE to dementia risk but not s |
| 568 | Participation in Pre-High School Football and Neurological, Neuroradiological, and Neuropsychological Findings in Later Life: A Study of 45 Retired National Football League Players | Not assessing for sport and cli |
| 585 | Tau-PET in a Former American Football Player with Pathologically Confirmed Chronic Traumatic Encephalopathy | Full-text not accessible. |
| 596 | Association Between Playing American Football in the National Football League and Long-term Mortality | Not assessing for sport and cli |
| 653 | Association of Cavum Septum Pellucidum and Cavum Vergae With Cognition, Mood, and Brain Volumes in Professional Fighters | Not assessing for sport and cli |
| 657 | Longitudinal change in regional brain volumes with exposure to repetitive head impacts | Not assessing for sport and cli |
| 659 | DURATION OF AMERICAN FOOTBALL PLAY AND CHRONIC TRAUMATIC ENCEPHALOPATHY | Not assessing for sport and cli |

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| 697 | Fluid biomarkers and risk of neurodegenerative disease in retired athletes with multiple concussions: results from the International Concussion and Head Injury Research Foundation Brain health in Retired athletes Study of Ageing and Impact-Related Neurodegenerative Disease (ICHIRF-BRAIN study) | Not assessing for sport and cli |
| 700 | Association of Playing College American Football With Long-term Health Outcomes and Mortality | Age relevant details identified a<br><br>Not enough information to dete e.g. Median age 66 |
| 728 | Neuroimaging of Cognitive Dysfunction and Depression in Aging Retired National Football League Players A Cross-sectional Study | Not assessing for sport and cli |
| 756 | Chronic traumatic encephalopathy in boxers. | Full-text not accessible. |
| 772 | Examining for Cavum Septum Pellucidum and Ventricular Enlargement in Retired Elite-Level Rugby League Players | Not enough information to dete<br><br>Not assessing for sport and cli |
| 784 | Long-term health outcomes after exposure to repeated concussion in elite level: rugby union players | Not assessing for sport and cli |
| 849 | Neurodegenerative causes of death among retired National Football League players | Accepted<br><br>Looks at neurodegenerative m<br><br>90% of sample died before 70 partial comparisons. |
| 853 | Chronic Effects of Boxing: Diffusion Tensor Imaging and Cognitive Findings | Not assessing for sport and cli |
| 992 | NZ-RugbyHealth Study: Self-reported Injury Experience and Current Health of Former Rugby Union and Non-contact Sport Players | Not assessing for sport and cli |
| 1062 | Neurodegenerative disease among male elite football (soccer) players in Sweden: a cohort study | Accepted. |
| 1077 | Neurodegenerative Disease Mortality among Former Professional Soccer Players | Replication data of Russell (20 |
| 1091 | | Full text not in English. |
| 1122 | | Full-text not accessible. |
| 1259 | Life Expectancy of White and Non-White Elite Heavyweight Boxers | Not assessing for sport and cli<br><br>Included ‘neurological disorder |
| 1373 | A retrospective analysis of all-cause and cause-specific mortality rates in French male professional footballers | Not enough information to dete |
| 1390 | All-cause and disease-specific mortality among male, former elite athletes: an average 50-year follow-up | Not assessing for sport and cli |

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| 1411 | Longitudinal Changes in Regional Brain Volumes and Cognition of Professional Fighters With Traumatic Encephalopathy Syndrome. | Not assessing for sport and cli |
| 1434 | Potentially modifiable dementia risk factors in all Australians and within population groups: an analysis using cross-sectional survey data. | Participants not associated wit |
| 1453 | Neuropsychological test performance of former American football players. | Not assessing for sport and cli |
| 1454 | Mortality risk factors among National Football League players: An analysis using player career data. | Not assessing for sport and cli |
| 1466 | Assessing Clinical Change in Individuals Exposed to Repetitive Head Impacts: The Repetitive Head Impact Composite Index. | Not assessing for sport and cli |
| 1467 | Effect of Weight Class on Regional Brain Volume, Cognition, and Other Neuropsychiatric Outcomes among Professional Fighters. | Not assessing for sport and cli |
| 1522 | Relating American Football Age of First Exposure to Patient-Reported Outcomes and Medical Diagnoses Among Former National Football League Players: An NFL-LONG study. | Accepted |
| 1557 | Relationship Between Level of American Football Playing and Diagnosis of Chronic Traumatic Encephalopathy in a Selection Bias Analysis. | Not assessing for sport and cli |
| 1569 | Neurodegenerative disease risk among former international rugby union players. | Not enough information to dete |
| 1661 | Age at League Entry and Early All-Cause Mortality among National Football League Players. | Not assessing for sport and cli |
| 1687 | Association of Field Position and Career Length With Risk of Neurodegenerative Disease in Male Former Professional Soccer Players. | Accepted. |
| 1695 | Exposure to Repetitive Head Impacts Is Associated With Corpus Callosum Microstructure and Plasma Total Tau in Former Professional American Football Players. | Not assessing for sport and cli |
| 1725 | Association of Position Played and Career Duration and Chronic Traumatic Encephalopathy at Autopsy in Elite Football and Hockey Players. | Not assessing for sport and cli |
| 1866 | Association between contact sports participation and chronic traumatic encephalopathy: a retrospective cohort study. | Not assessing for sport and cli |
| 1918 | Football's InfluencE on Lifelong health and Dementia risk (FIELD): protocol for a retrospective cohort study of former professional footballers. | No primary data, summary stat |
| 1989 | Lewy Body Pathology and Chronic Traumatic Encephalopathy Associated With Contact Sports. | Not assessing for sport and cli |

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| | | CTE – Lewy Body risk, not den |
| 2027 | The relationship between brain atrophy and cognitive-behavioural symptoms in retired Canadian football players with multiple concussions. | Not assessing for sport and clin |
| 2099 | CCL11 is increased in the CNS in chronic traumatic encephalopathy but not in Alzheimer's disease. | Not enough information to dete<br><br>Not assessing for sport and clin |
| 2103 | A history of concussions is associated with symptoms of common mental disorders in former male professional athletes across a range of sports. | Not assessing for sport and clin |
| 2107 | Large case series documents chronic brain damage in players of American football. | Not an original piece of researc |
| 2153 | High School Football and Late-Life Risk of Neurodegenerative Syndromes, 1956-1970. | Not enough information to dete |
| 2176 | Cumulative Head Impact Exposure Predicts Later-Life Depression, Apathy, Executive Dysfunction, and Cognitive Impairment in Former High School and College Football Players. | Not assessing for sport and clin |
| 2225 | [Late-onset Neurodegenerative Diseases Following Traumatic Brain Injury: Chronic Traumatic Encephalopathy (CTE) and Alzheimer's Disease Secondary to TBI (AD-TBI)]. | Full-text not accessible. |
| 2302 | Chronic traumatic encephalopathy pathology in a neurodegenerative disorders brain bank. | Not enough information to dete<br><br>Not an observational study<br><br>Not assessing for sport and clin |
| 2323 | Beta-amyloid deposition in chronic traumatic encephalopathy. | Not assessing for sport and clin<br><br>CTE – Dementia risk rather tha |
| 2455 | Prevalence and characterization of mild cognitive impairment in retired national football league players. | Cannot determine dementia dia |
| 2536 | High school football and risk of neurodegeneration: a community-based study. | Not enough information to dete<br><br>[median age 72] |
| 2563 | [Dementia pugilistica]. | No primary data/summary stati |
| 2611 | TDP-43 proteinopathy and motor neuron disease in chronic traumatic encephalopathy. | Not assessing for sport and clin |
| 2646 | [Sports medicine: Mr Hyde and Dr.Jekyll! ]. | Full-text not accessible. |
| 2742 | Association between recurrent concussion and late-life cognitive impairment in retired professional football players. | Accepted |
| 2778 | A 9-year controlled prospective neuropsychologic assessment of amateur boxing. | Not assessing for sport and clin<br><br>[Assesses risk of CTE with box |

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| 2840 | Controlled prospective neuropsychological assessment of active experienced amateur boxers. | Not assessing for sport and cli<br><br>[Assesses risk of CTE with box |
| 2874 | Does Swedish amateur boxing lead to chronic brain damage? 2. A retrospective study with CT and MRI. | Not assessing for sport and cli |
| 2922 | Cognitive Impairment and Self-Reported Dementia in UK Retired Professional Soccer Players: A Cross Sectional Comparative Study. | Accepted. |
| 2926 | American Football Play and Parkinson Disease Among Men. | Not enough information to dete<br><br>Not assessing for sport and cli<br><br>[Idiopathic Parkinson's Disease |
| 2929 | Heading Frequency and Risk of Cognitive Impairment in Retired Male Professional Soccer Players. | Accepted. |
| 2942 | Association of white matter rarefaction, arteriolosclerosis, and tau with dementia in chronic traumatic encephalopathy | Not enough information to dete |
| 2958 | Heading in football, long-term cognitive decline and dementia: evidence from screening retired professional footballers. | Not enough information to dete<br><br>[Stratified ages were provided |
| 2983 | Amateur Boxing and Dementia: Cognitive Impairment Within the 35-Year Caerphilly Cohort Study. | Medical records for dementia w |
| 2988 | Mild Cognitive Impairment and Dementia Reported by Former Professional Football Players over 50 yr of Age: An NFL-LONG Study. | Accepted. |
| 3012 | A Preliminary Study of Early-Onset Dementia of Former Professional Football and Hockey Players. | Accepted. |
| 3062 | Alzheimer's disease and chronic traumatic encephalopathy: Distinct but possibly overlapping disease entities. | Not an observational study. |
| 3071 | Cognitive ability in former professional football (soccer) players is associated with estimated heading frequency | Not enough information to dete<br><br>Not assessing for sport and cli |
| 3088 | Association of Adverse Childhood Experiences With Poor Neuropsychiatric Health and Dementia Among Former Professional US Football Players. | Not assessing for sport and cli<br><br>[Assesses risk of dementia fro<br>Experiences, rather than partic |
| 3102 | Cerebrospinal fluid tau, aβ, and sTREM2 in Former National Football League Players: Modeling the relationship between repetitive head impacts, microglial activation, and neurodegeneration | Not assessing for sport and cli |
| 3295 | HOW PUNCHING HAS CHANGED IN THE SPORT OF BOXING. | Full-text not accessible. |

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| 3395 | Association of probable REM sleep behavior disorder with pathology and years of contact sports play in chronic traumatic encephalopathy | Not assessing for sport and cli<br><br>[CTE-Dementia + Lewy Body a association]. |
| 3414 | Study Points to Characteristic Pattern of Protein Deposits in Brains of Retired NFL Players Who Suffered Concussions. | Full-text not accessible. |
| 3497 | Cognitive and psychosocial function in retired professional hockey players | Not enough information to dete<br><br>Not assessing for sport and cli |
| 3650 | Lack of Association of Informant-Reported Traumatic Brain Injury and Chronic Traumatic Encephalopathy | Not an observational study. |
| 3657 | Inflammatory biomarkers for neurobehavioral dysregulation in former American football players: findings from the DIAGNOSE CTE Research Project | Not assessing for sport and cli |
| 3665 | Chronic traumatic encephalopathy neuropathologic change in former Australian rugby players | Not enough information to dete<br><br>Not assessing for sport and cli |
| 3676 | Blood biomarkers and neurodegeneration in individuals exposed to repetitive head impacts | Not assessing for sport and cli |
| 3804 | Linking Type and Extent of Head Trauma to Cavum Septum Pellucidum in Older Adults With and Without Alzheimer Disease and Related Dementias. | Not enough information to dete |
| 3859 | Amyloid PET across the cognitive spectrum in former professional and college American football players: findings from the DIAGNOSE CTE Research Project. | Not assessing for sport and cli |
| 3897 | Chronic Traumatic Encephalopathy in Soccer Players: Review of 14 Cases. | Not an original piece of researc |
| 3921 | New Criteria Can Identify Who May Develop CTE Among Professional Fighters. | Full-text not accessible |
| 3931 | Chronic Traumatic Encephalopathy Found Post-mortem in Young Athletes Who Played Contact Sports. | Not enough information to dete<br><br>Not assessing for sport and cli |
| Manual | Kumanu Tāngata—The Aftermatch Project: Neurodegenerative Disease Epidemiology in Former First-Class New Zealand Rugby Players | Not enough information to dete<br><br>[No <64 year data.] |
| Manual | Environmental Risk Factors for Early-Onset Alzheimer's Dementia and Frontotemporal Dementia: A Case-Control Study in Northern Italy | Accepted. |
| 3990 | Clinical implications of head trauma in frontotemporal dementia and primary progressive aphasia | Not enough information to dete |
| 3995 | Younger Age of First Exposure to American Football is Associated with Worse Informant-Reported Clinical Outcomes in Older Age | Not original piece of research ( |
| 3998 | Tau Pathology in Alzheimer's Disease and Other Dementias – Translational Approach From in Vitro Autoradiography to in Vivo Pet Imaging | No primary data |

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| 4001 | The Effect of Repetitive Sub-Concussive Head Impacts in a Rodent Model and Its Implication in Contact Sports | No primary data. |
| 4026 | Multiparameter cortical surface morphology in former amateur contact sport athletes | Not assessing for sport and cli |
| 4041 | Genomic Studies in Chronic Traumatic Encephalopathy (CTE): From External Traumas to Genetic Alterations | No primary data |
| 4047 | Substantia Nigra Pathology, Contact Sports Play, and Parkinsonism in Chronic Traumatic Encephalopathy | Not assessing for sport and cli |
| 4056 | Associations between repetitive head impact exposure and midlife mental health wellbeing in former amateur athletes | Not assessing for sport and cli |
| 4061 | Beyond Traditional Measures: Exploring Cognitive Intraindividual Variability in Traumatic Encephalopathy Syndrome | Not assessing for sport and cli |
| 4067 | Clinical Manifestations. | Not assessing for sport and cli |
| 4200 | Repeated Head Trauma May Lead to Parkinsonism in Patients with CTE. | Full-text not assessable. |
| 4203 | Health and Lifestyle Factors and Dementia Risk Among Former Professional Soccer Players. | Not enough information to dete |
| 4539 | Biomarker evidence of neurodegeneration in mid-life former rugby players | Dementia rates are not analyse |

**Appendix 6 – Sensitivity Analysis**

| Exposure | | | | Outcome | | Population | | | Summary of Findings | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Author (Year, country), study design** | **Sport (Amateur/Professional)** | **Mean career length (SD)** | **Concussion/ Head injury info.** | **Dementia type.** | **Nature of recording.** | **Exposure group cases of exposure/total cases** | **Comparison cases of exposure/total cases** | **Age Related Info.** | **Age-adjusted OR's/ HR's (95% CI) or PR/SMR/PPE/% - Significant results in bold.** | **Quality/Risk of Bias** | **Comments** |
| Russell (2021, UK), cohort. | Soccer (Professional) | 8.6 (6.2) | Not Measured. | Neurodegenerative Disease and Dementia NOS. | Death certification; Hospital Records; Prescriptions. | Total 30,704<br><br>Exposure group: 386/7676 | Matched population control: 366/23,028<br><br>Year of birth (n/total n):<br><br>1910-1929 (53/543)<br><br>1930-1949 (188/4,677) | Year of births (n/total n):<br><br>1910-1929 (61/181)<br><br>1930-1949 (219/1,559)<br><br>1950-1969 (34/3,403) | 1950-1969 HR: 5.11 (2.77-9.43), p<0.001<br><br>1930-1949: 3.66(2.85-4.69), p<0.001<br><br>1910-1929: 3.78(2.26-6.35), p<0.001 | | All ages showed significant positive effect with youngest age-group showing largest effect compared to matched controls. |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 1950-1969 (22/10,206) | | | | |
| Ueda (2023, Sweden) - Cohort | Soccer (Professional) | Not assessed. | N/A | “Alzheimer’s Disease and other dementias” | Hospital and death records. | Football cohort n/total n = 537/6007<br><br>1924-39 (130/1017)<br>1940-49 (142/640)<br>1950–59 (168/688)<br>1960-69 (78/651)<br>1970-2019 (19/3011) | Population matched controls - n/total n = 3485/56,168<br><br>1924-39 (994/9665)<br>1940-49 (898/5920)<br>1950-59 (997/6068)<br>1960-69 (401/5950)<br>1970-2019 (195/28565) | Stratified Ages based on year of first season in top division. | HR’s by year of first season:<br><br>1924-39: 1.45 (1.20-1.74) <0.0001<br>1940-49 - 1.58 (1.32-1.89) <0.0001<br>1950-59 - 1.42 (1.21-1.68) <0.0001<br>1960-69 - 1.59 (1.25-2.03) 0.0002<br>1970-2019 - 0.90 (0.56-1.45) 0.678 | Tentatively suggests younger cohorts have lower risk of neurodegenerative disease compared to matched population controls. However non-significant results and small effect. |

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|---|---|---|---|---|---|---|---|---|---|---|
| Lehman (2012, UK), cohort. | NFL (Professional) | N/A | Sped group (higher concussions): 14/173<br><br>Non-sped group (lower concussions): 3/152 | Dementia/Alzheimer's Disease | Mortality Records in 2 groups:<br><br>Underlying cause<br><br>Contributing cause /MCOD (Multiple Cause of Death). | Total deaths: 10/334<br><br>Speed group: 14/173<br><br>Non-speed group: 3/152 | US Population comparison | Median age at death 54 (27-81) | Overall SMR: 0.53 (0.48-0.59); Neurodegenerative underlying cause SMR: 2.83 (1.36-5.21); MCOD SMR: 3.26(1.90-**5.22);** AD MCOD **SMR: 3.86(1.55-7.95)**<br><br>For speed position (median age at death 54): Neurodegenerative Disease **OR 4.74(2.59-7.95);** AD: **6.02(2** | All-cause mortality lower but neurodegenerative mortality 3-times higher despite the low average age of sample. Suggests 'healthy-worker' effect may not be age-related.<br><br>High age range limits the relevance to young-onset dementia. |

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13.1)

## Appendix 7: Study Checklist

| Section and Topic | Item # | Checklist item |
|---|---|---|
| **TITLE** | | |
| Title | 1 | Identify the report as a systematic review. |
| **ABSTRACT** | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. |
| **INTRODUCTION** | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. |
| **METHODS** | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the synthe |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched o date when each source was last searched or consulted. |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and lim |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including and each report retrieved, whether they worked independently, and if applicable, details of automation |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data fr independently, any processes for obtaining or confirming data from study investigators, and if applicab process. |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compati study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decid |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention charact assumptions made about any missing or unclear information. |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) study and whether they worked independently, and if applicable, details of automation tools used in th |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating comparing against the planned groups for each synthesis (item #5)). |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of conversions. |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-ana model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software pack |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. sub |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from re |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcom |

| Section and Topic | Item # | Checklist item |
|---|---|---|
| **RESULTS** | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the s the review, ideally using a flow diagram. |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why |
| Study characteristics | 17 | Cite each included study and present its characteristics. |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) a (e.g. confidence/credible interval), ideally using structured tables or plots. |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized result |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each syn |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. |
| **DISCUSSION** | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. |
| | 23b | Discuss any limitations of the evidence included in the review. |
| | 23c | Discuss any limitations of the review processes used. |
| | 23d | Discuss implications of the results for practice, policy, and future research. |
| **OTHER INFORMATION** | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or sta |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or spo |
| Competing interests | 26 | Declare any competing interests of review authors. |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collec studies; data used for all analyses; analytic code; any other materials used in the review. |