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Dementia in former amateur and professional contact sports participants: population-based cohort study, systematic review, and meta-analysis

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Summary

Background Although there is growing evidence that former professional athletes from sports characterised by repetitive head impact subsequently experience an elevated risk of dementia, the occurrence of this disorder in retired amateurs, who represent a larger population, is uncertain. The present meta-analysis integrates new results from individual-participant analyses of a cohort study of former amateur contact sports participants into a systematic review of existing studies of retired professionals and amateurs.

Methods The cohort study comprised 2005 male retired amateur athletes who had competed internationally for Finland (1920–1965) and a general population comparison group of 1386 age-equivalent men. Dementia occurrence was ascertained from linked national mortality and hospital records. For the PROSPERO-registered (CRD42022352780) systematic review, we searched PubMed and Embase from their inception to April 2023, including cohort studies published in English that reported standard estimates of association and variance. Study-specific estimates were aggregated using random-effect meta-analysis. An adapted Cochrane Risk of Bias Tool was used to assess study quality.

Findings In the cohort study, up to 46 years of health surveillance of 3391 men gave rise to 406 dementia cases (265 Alzheimer's disease). After adjustment for covariates, former boxers experienced elevated rates of dementia (hazard ratio: 3.60 [95% CI 2.46, 5.28]) and Alzheimer's disease (4.10 [2.55, 6.61]) relative to general population controls. Associations were of lower magnitude in retired wrestlers (dementia: 1.51 [0.98, 2.34]; Alzheimer's disease: 2.11 [1.28, 3.48]) and soccer players (dementia: 1.55 [1.00, 2.41]; Alzheimer's disease: 2.07 [1.23, 3.46]), with some estimates including unity. The systematic review identified 827 potentially eligible published articles, of which 9 met our inclusion criteria. These few retrieved studies all sampled men and the majority were of moderate quality. In sport-specific analyses according to playing level, there was a marked difference in dementia rates in onetime professional American football players (2 studies; summary risk ratio: 2.96 [95% CI 1.66, 5.30]) relative to amateurs in whom there was no suggestion of an association (2 studies; 0.90 [0.52, 1.56]). For soccer players, while dementia occurrence was raised in both erstwhile professionals (2 studies; 3.61 [2.92, 4.45]) and amateurs (1 study; 1.60 [1.11, 2.30]) there was again a suggestion of a risk differential. The only studies of boxers comprised former amateurs in whom there was a tripling in the rates of dementia (2 studies; 3.14 [95% CI 1.72, 5.74]) and Alzheimer's disease (2 studies; 3.07 [1.01, 9.38]) at follow-up compared to controls.

Interpretation Based on a small number of studies exclusively sampling men, former amateur participants in soccer, boxing, and wrestling appeared to experience an elevated risk of dementia relative to the general population. Where data allowed comparison, there was a suggestion that risks were greater amongst retired professionals relative to amateurs in the sports of soccer and American football. Whether these findings are generalisable to the contact sports not featured, and to women, warrants examination.

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Research in context

Evidence before this study

There is some evidence that former professional contact sports athletes subsequently experience greater rates of dementia than unexposed controls, but whether disease rates are also elevated in former amateurs, who participate in larger numbers, is uncertain. Searching electronic databases using terms for specific contact sports (e.g., 'soccer, 'wrestling') and dementia outcomes (e.g., 'dementia', 'Alzheimer') revealed only three qualifying studies for former soccer players and one on retired boxers with follow-up for dementia. There were no data on studies of erstwhile wrestlers, nor any meta-analysis offering a quantification of dementia risk according to professional versus amateur status.

Added value of this study

Taking new results from individual-participant analyses of a cohort of retired amateur athletes together with the existing literature, former amateur participants in soccer (1 study), boxing (2 studies), and wrestling (1 study) appeared to experience an elevated risk of dementia relative to the general population. Where data allowed comparison, there was a suggestion that risks were greater amongst retired professionals relative to amateurs in the sports of soccer and American football.

Implications of all the available evidence

With soccer being the most common participation sport worldwide and wrestling long-established in the educational systems of selected countries, that the risk of dementia appears to be elevated in amateur playing groups from these sports—albeit based on a very small cluster of studies—has potential public health relevance if replicated in new studies.

Introduction

Estimates of the considerable present and future burden of dementia for individuals, societies, and health care systems are well-documented.[1] Unsuccessful trials of drug treatments to alter the course of the disease brings into sharp focus the need to identify modifiable risk factors for the primary prevention of dementia.[2] In people who experience head trauma serious enough to warrant hospitalisation, large scale cohort studies of the general population indicate an approximate doubling in the rate of later dementia relative to the unexposed.[3–6] These observations raise the possibility that lower intensity repetitive head impact, characteristic of participation in contact sports, may also have long-term implications for brain health and there is some recent evidence that this is the case.[7]

Retired professional soccer players, for instance, have a higher occurrence of dementia and Alzheimer's disease relative to the general population.[8,9] This risk differential has also been reported for former American footballers,[10,11] although this is not a universal observation.[12] With the majority of this literature focusing on retired professional athletes, the risk to former amateur sports people is uncertain. If dementia occurrence is also elevated in onetime amateur athletes, the population impact will be higher as these groups participate in greater numbers.[7]

To explore dementia risk according to former professional versus amateur status, we first utilise new data from a well-characterised cohort study of men drawn from an array of elite amateur athletic backgrounds which include the contact sports of soccer, wrestling, and boxing, who had long-term follow-up for incident dementia. We then integrate these results into a meta-analysis based on a systematic review of results from all published cohort studies. While other systematic reviews exist,[13–15] to the best of our knowledge, this is first meta-analysis of dementia rates in former contact sports participants.

Methods

Cohort of Finnish former elite athletes and population controls

This cohort study was initiated in 1978 to examine the relationship between participation in sports and long-term health.[16–19] In brief, former athletes were selected based on the following criteria: male; represented Finland 1920–1965 on at least one occasion in the Olympic games, World or European championships, or intercountry competitions; and competed in the sports of track and field athletics, cross-country skiing, soccer, ice hockey, basketball, boxing, wrestling, weight-lifting, or shooting. Full name, and place and date of birth were extracted from sports yearbooks and registers of sports associations and, if necessary, enquiries were made to relatives, friends, sports journals, and Finnish embassies abroad. This process resulted in a group of 2613 men and represented the athlete cohort.

During the same period in which the athlete cohort was established, an external, general population-based comparison group of 1712 men was selected from the male Finnish population who, at the age of 20 years, were classified as healthy at their medical examination for induction into military or civic service, and who were in the same age cohort and area of residence as the athletes. Practically, after first finding the athlete in the population register, the nearest control matching these inclusion criteria was then chosen.

Data collection was approved by the ethics committee of the Hospital Districts of Helsinki and Uusimaa, and all participants consented. The presentation of this cohort study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement of guidelines for reporting observational studies.[20]

Derivation of exposed and unexposed groups

We attempted to categorise sports based on frequency of all head impacts, however, in the absence of such data we used results for concussion occurrence as a proxy (summarised in Supplemental Table S1).[21–23] Contact sports were classified as soccer, boxing, wrestling, ice hockey, and basketball, and non-contact as track and field, cross-country skiing, and weight-lifting. Individual contact sports were then disaggregated as the numbers of dementia cases at follow-up permitted. Thus, separate analyses were possible for former soccer players, boxers, and wrestlers (freestyle/Greco-Roman), while retired athletes from the sports of ice hockey and basketball players were combined into an 'other' contact sports category.

Assessment of covariates

Data on covariates were extracted from two sources. The presence of diabetes, hypertension, and coronary heart disease was derived from linkage of study members to a national drug treatment register. Additionally, in 1985, surviving study members and population controls (N = 2851; 66% of the original cohort) were mailed a self-completion questionnaire (N = 1917; response 67%) (Supplemental Fig. S1) with enquiries regarding health behaviours (smoking, alcohol intake), physical stature, and weight. Body mass index was computed using the usual formulae.[24] Questionnaire data in combination with those extracted from the Finnish Central Population Registry were used to generate a variable for longest held occupation, our indicator of socioeconomic status.[25]

Ascertainment of dementia

Health surveillance began upon initiation of nationwide health registries in 1970 when the average age of the athlete group was 45.4 years (controls 44.3 years). Study members were linked to: death records, including cause; hospitalisation records, including cause; and the Finnish Drug Prescription Register for medications specifically used to treat Alzheimer's disease (linkage from 1995). See Supplemental Table S2 for International Classification of Disease and medication codes. Using these data, we derived three dementia outcomes for use in the present analyses: dementia, Alzheimer's disease, and non-Alzheimer's dementia.

Systematic review and meta-analysis

Search strategy and study selection

This PROSPERO-registered (CRD42022352780) systematic review and meta-analysis was reported in accordance with the guidelines for Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)[26] and Meta-analysis Of Observational Studies in Epidemiology (MOOSE).[27] We identified relevant literature by searching PubMed (Medline) and Embase databases between their inception and April 23 2023. We used combinations of free text and controlled terms in 2 categories (Supplemental Box S1): the exposure (i.e., specific sports such as boxing, soccer, martial arts, and rugby), and the outcome (i.e., dementia and its subtypes such as Alzheimer's disease and vascular dementia). We also scrutinised the reference sections of retrieved articles.

We included a published paper if it fulfilled the following criteria: utilised a cohort study design; a comparison of dementia occurrence was made between a group of former contact sports athletes and unexposed (general population) or lesser-exposed (former athletes from non-contact sports) controls; the diagnosis of dementia outcomes was made by a healthcare professional as part of a medical examination in either a research or clinical setting (studies based on self-reports of physician diagnosis and cognitive tests did not qualify); reported standard estimates of association (e.g., relative risk, odds ratios, hazard ratios) and variance (e.g., confidence interval, standard error); appeared in a peer-reviewed journal; and was published in English. Two authors (GDB and PF) independently screened the identified records first by title, then abstract, and, if necessary, the full paper. Any discrepancies were resolved on discussion.

Extraction of results and assessment of study quality

Where available, a range of characteristics were extracted from each publication, including the name of the lead author, publication year, country of sample population, number of participants in exposed and unexposed groups, number of events and type, and effects estimates from both minimally- and multivariable-adjusted analyses. Study authors were contacted when clarification was required.

We classified sports participation as professional (salaried) or amateur (non-salaried). We reasoned that individuals who were professional—that is, for whom sport was their primary occupation—would be exposed to a greater number of head impacts in training and probably competition. Contrary to most present-day sports, elite participation in the early- to mid-20th century, was rarely professional (salaried). For context, for those athletes who achieved the pinnacle of their sport by representing their country in the Olympic games, this would have been on an amateur basis prior to 1986 when professional athletes were finally admitted.

We used an adapted version of the Cochrane Risk of Bias Tool to quantify study quality.[28] This comprised seven domains of appraisal, including the comprehensiveness of the exposure, confounding variables, outcome ascertainment, and adequacy of the follow-up (Supplemental Table S3). With a maximum of 4 points for each domain (total 28), we regarded the quality of the study as high if the total score was at least 21, moderate if the score ranged between 14 and 20, and low if it was <14.

Statistical analyses

In individual-participant analyses of the Finnish cohort study, after exclusion of study members owing to record-linkage failure and death prior to the beginning of follow-up. Event surveillance was from 1st January 1970 until the occurrence of a dementia event or the end of surveillance (December 31, 2015)—whichever came first. Having ascertained that the proportional hazards assumption had not been violated, we used Cox regression to compute hazard ratios with accompanying 95% confidence intervals to summarise the relationship of a background in contact sports with the risk of dementia and related outcomes.[29] Age was used as the time covariate in the most basic model, with other covariates subsequently added, including indicators of socioeconomic status, co-morbidity, and health behaviours, all of which have been linked to dementia risk.[30] To model competing risks, we used the method described by Fine & Gray.[31] In these analyses the competing risk was mortality from cardiovascular disease as the underlying cause of death (ICD-10 codes I00–I99, or the equivalent in ICD-9 or ICD-8).

We then pooled the results from the analyses of raw data in the Finnish cohort alongside published study-specific estimates using a random effects meta-analysis,[32] an approach which incorporates the heterogeneity of effects in the computation of their aggregation. An I^2 statistic was used to summarise the heterogeneity in estimates across studies. To be included in the meta-analysis, there needed to be at least 2 studies with independent samples from the same sport. All analyses were computed using Stata 15 (StataCorp, College Station, TX) and analytical codes for the main analyses of the Finnish cohort are provided in Supplemental Box S2.

Role of the funding source

This report had no direct funding. All authors had final responsibility for the decision to submit for publication.

Results

Finnish cohort study

Relative to general population controls, Finnish elite sports participants had marginally more favourable baseline risk factor profiles at follow-up (Supplemental Table S4). These differentials were most consistently evident for socio-economic disadvantage and cigarette smoking. In contrast, heavy alcohol consumption was generally more common in the athletes.

In these analyses a mean of 30.6 years of disease surveillance (range 1–46) in an analytical sample of 3391 men (2005 former athletes, 1386 controls) gave rise to 406 cases of dementia (265 cases of Alzheimer's disease). As anticipated, several of these baseline characteristics were related to an elevated rate of dementia (Supplemental Table S5), although statistical significance at conventional levels was not always apparent. Thus, there was around a 50% increase in the risk of future dementia if study members came from poor social circumstances (age-adjusted hazard ratio; 95% confidence interval: 1.70; 1.25, 2.31), had a physical morbidity such as diabetes (1.50; 1.15, 1.97) or hypertension (1.41; 1.15, 1.73), smoked cigarettes (1.41; 1.01, 1.98), or lost consciousness at least annually owing to heavy alcohol intake (1.69; 1.23, 2.33). There was, however, an absence of association for existing heart disease, being unmarried, and being overweight or obese.

In the analyses of contact sports participation and dementia risk, with there being little difference in the magnitude of the hazard ratios in the univariate and multivariate models (Table 1) we present the results for the latter here. Former amateur boxers experienced a more than three-fold risk of dementia (hazard ratio 3.60 [95% CI 2.46, 5.28]) relative to the general population comparison group. While risk was also elevated in retired wrestlers (1.51 [0.98, 2.34]) and soccer players (1.55 [1.00, 2.41]), statistical significance was not apparent. The risk of dementia in erstwhile athletes from 'other' contact sports (ice hockey and basketball) and those from non-contact sports such as track and field was not significantly different to the general population controls. Alzheimer's disease was most strongly related to a history of contact sports, whereby a background in amateur boxing was associated with a quadrupling in risk (4.10 [2.55, 6.61]), and the rate in wrestlers (2.11 [1.28, 3.48]) and soccer players (2.07 [1.23, 3.46]) was around double that of general population controls. The risk of non-Alzheimer's dementia was also raised in retired amateur boxers (2.62; 1.68, 4.11) but not convincingly so in former soccer players (1.23 [0.74, 2.06]) nor wrestlers (1.22 [0.73, 2.03]) (Supplemental Table S6).

Study members reported their career duration in the questionnaire administered in 1985. There was a suggestion that boxers who fought competitively for 15 years or more had twice the rate of Alzheimer's disease (2.07; 0.95, 4.51) relative to those with shorter

	n/N	Dementia		Alzheimer's disease	
		Age-adjusted (406/3391)	Age-, SES-, co-morbidity, and lifestyle factors-adjusted (288/1916)	Age-adjusted (265/3391)	Age-, SES-, co-morbidity, and lifestyle factors-adjusted (188/1917)
Boxing	64/230	3.68 (2.72, 4.99)	3.60 (2.46, 5.28)	4.45 (3.07, 6.45)	4.10 (2.55, 6.61)
Wrestling	38/247	1.31 (0.91, 1.89)	1.51 (0.98, 2.34)	1.90 (1.24, 2.90)	2.11 (1.28, 3,48)
Soccer	44/248	1.80 (1.27, 2.54)	1.55 (1.00, 2.41)	2.43 (1.62, 3.64)	2.07 (1.23, 3.46)
Other contact sports	18/236	0.74 (0.45, 1.22)	0.73 (0.41, 1.30)	0.85 (0.46, 1.56)	0.80 (0.39, 1.62)
Non-contact sports	122/1044	0.88 (0.68, 1.13)	0.80 (0.58, 1.11)	0.89 (0.64, 1.23)	0.84 (0.55, 1.28)
General population (controls)	120/1386	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)

n = number of events; N = group size. Number of events and group size according to individual sports are for age-adjusted analyses of dementia. SES, socioeconomic status. Co-morbidities are diabetes, hypertension, and coronary heart disease. Lifestyle factors are alcohol intake, passing out due to alcohol, body mass index, and smoking status.

Table 1: **Hazard ratios (95% confidence intervals) for the association of former participation in contact sports with dementias and Alzheimer's disease: Finnish cohort study.**

exposures, although, again, confidence intervals included unity; no such differential was apparent for wresting or soccer, however (Supplemental Table S7).

We conducted some sensitivity analyses. First, given the maturity of this cohort, competing risk bias may arise because the occurrence of a non-dementia event precludes occurrence of our primary outcome of interest. We therefore subjected Alzheimer's disease to a competing risks analysis based on the most common cause of ill-health herein—cardiovascular disease—and our findings were unchanged (Supplemental Table S8). Second, given the amateur era in which study members competed internationally, it is plausible that, if sufficiently skilled, they could have participated at elite level in more than one of the sports linked to dementia in our analyses. Mutual control for each of the three sports related to dementia in earlier analyses did not, however, alter the overall pattern of association (Supplemental Table S9). Third, owing to missing data, the more complex statistical models (age-, SES-, co-morbidity, and lifestyle factors) comprise fewer study members (N = 1917 in the analyses of Alzheimer's disease) than the model only featuring age (N = 3391). We therefore recomputed the main effects in a non-missing dataset and the multiply-adjusted results were essentially the same (Supplemental Table S10). Fourth, although men in the athlete groups were excluded from the population control cohort, it is plausible that the latter still contained some people who had participated at lower levels in the sports linked to dementia in the present study. While this misclassification would have had the impact of lowering the risk ratio for dementia when comparing the contact sport group with the population controls, we nonetheless tested the impact, if any, of this potential bias. A total of 66 of the 765 men in the control group who returned a questionnaire in 1985 indicated they had participated as young adults in one of three collision sports associated with neurodegenerative disease in the present study, however, when they were excluded from the control group there was no change to the results (Supplemental Table S11). Lastly, we examined the impact of the later availability of the medication registry for Alzheimer's disease (1995 versus 1970 for deaths and hospitalisation). Unsurprisingly, there was some overlap between these three health registries but only 15 of 265 Alzheimer's disease cases were based solely on medication data. To quantify any impact if this differential availability of these data over time, we recoded our Alzheimer's disease outcome. In relation to sports participation, Alzheimer's disease ascertainment based on the three registers (death, hospitalisation, and medication) revealed very similar results to this health outcome when data on medication were dropped (Supplemental Table S12).

Systematic review and meta-analysis

The systematic review identified 827 potentially eligible published articles of which 9 met the inclusion criteria (Fig. 1). All retrieved studies exclusively comprised men, and represented cohorts of former amateurs,[12,33–35] professionals,[8–11] or, rarely, both.[36] Of these, four cohort studies captured dementia cases in retired American football players[10–12,33] (none featured Alzheimer's disease); there were three such studies of former soccer players[8,9,36] (one featured Alzheimer's disease[8]); one study of retired boxers[34] (one featured Alzheimer's disease[34]); and one of erstwhile rugby players[35] (Alzheimer's disease not featured) (Table 2). One study was field-based[34] while the remainder were generated from linkage of administrative records. Comparison groups were typically the general population, with two utilising a non-collision sports group.[11,12] The studies of erstwhile American football players were unsurprisingly based on samples from the USA,[10–12,33] whereas former boxers were drawn from Wales,[34] soccer players from Scotland,[8] France,[9] and Sweden,[36] and rugby union players from Scotland.[35] Where the details were made available by study authors, the number of events in the retired athletes ranged from 5[34] to 491[36] for dementia; 2[34] to 64[8] for

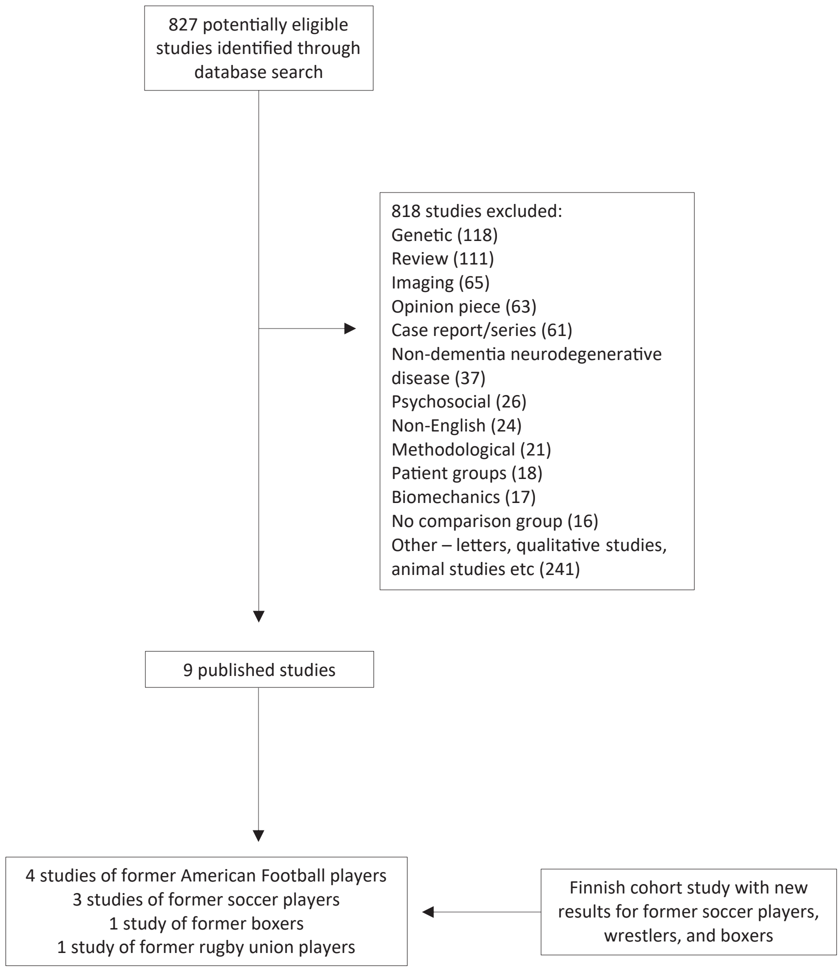

Fig. 1: **Study selection: systematic review.**

Alzheimer's disease; and for the single study reporting non-Alzheimer's dementia the count was 64.[8] Of the nine retrieved studies, only two[8,36] were evaluated as being of high quality; the remainder were moderate quality (Supplemental Table S3).

In analyses of specific sports, former soccer players experienced elevated rates of dementia (2.40 [1.48, 3.90]) and Alzheimer's disease (3.22 [1.34, 7.75]) (Fig. 2). Not shown in that figure, rates of non-Alzheimer's dementia, which included vascular dementia and Lewy body dementia, were also raised (2.32 [1.04, 5.16]). Confidence intervals around these estimates were typically wide, however, indicating low precision, and there was a high degree of cross-study heterogeneity in both analyses (I^2>81%). In the two studies of former professional soccer athletes, there was a greater risk of dementia (3.61 [2.92, 4.45]) relative to the single cohort of retired amateur players (1.60 [1.11, 2.30]). In the Swedish study (Ueda et al.[36]), which featured a combination of both playing levels, dementia risk (1.62 [1.47, 1.78]) was very close to that seen in the cohort of amateurs. In that study, most neurodegenerative disease events had occurred in the former amateur players because they represented the oldest study members (active 1924–1969; Peter Ueda, personal communication April 2023).

The overall results for the American football studies (Fig. 3) revealed a raised risk of dementia in former participants, the confidence interval for which included unity (1.63 [0.76, 3.49], I^2 = 75%). Again, however, a differential in dementia risk according to past playing level was also evident, whereby an association was apparent for retired professionals (2.96 [1.66, 5.30]) but not in onetime amateurs whose only exposure was in high school (0.90 [0.52, 1.56]). In one of the American football studies,[12] however, the 'unexposed' group of non-football players in fact comprised some wrestlers who, in analyses of the Finnish cohort study herein, had a modestly elevated post-retirement risk of dementia. This could have had the impact of narrowing the risk

Author (year of publication), study design	Exposed (unexposed group)	Country	Years active	Duration of follow-up	Number of exposed individuals (number of cases)	Number of unexposed individuals (number of cases)	Risk ratio (95% confidence interval) for exposed versus unexposed
American football							
Savica et al. (2012),[33] retrospective cohort study	Former high school (amateur) athletes (general population)	USA	1946–1956	Median 50.2 yr for athletes	438 (13 dementia deaths)	18.2 expected dementia deaths	0.72 (0.38, 1.23)
Lehman et al. (2012),[10] retrospective cohort study	Former professional athletes (general population)	USA	1959–1988	Median 57 yr for athletes	3439 (7 dementia)	NR	3.86 (1.55, 7.95)
Janssen et al. (2017),[12] retrospective cohort study	Former high school (amateur) athletes ('non-football' athletes)	USA	1956–1970	NR	296 (7 dementia/mild cognitive impairment)	190 (5 dementia/mild cognitive impairment)	1.29 (0.45, 2.32)
Nguyen et al. (2019),[11] retrospective cohort study	Former professional athletes (former baseball players)	USA	Football (1959–1988); baseball (1871–2006)	34 yr for athletes	3419 (16 dementia deaths)	2708 (10 dementia deaths)	2.26 (0.99, 5.17)
Soccer							
Mackay et al. (2019),[8] retrospective cohort study	Former professional athletes (general population)	Scotland	NR	NR	7676 former professional soccer players (180 dementia deaths, 64 from Alzheimer's disease)	23,028 members of general population (178 dementia deaths, 47 from Alzheimer's disease)	Dementia: 3.87 (2.86, 5.24), Alzheimer's disease: 5.07 (2.92, 8.82)
Orhant et al. (2022),[9] retrospective cohort study	Former professional athletes (general population)	France	1968–2015	Maximum 47 yr for athletes	6114 (47 dementia deaths)	13.9 expected dementia deaths	3.38 (2.49, 4.46)
Ueda et al. (2023),[36] retrospective cohort study	Former amateur and professional athletes (general population)	Sweden	1924–2019	Maximum of 50 years	6007 (491 dementia cases)	56,168 (2889 dementia cases)	1.62 (1.47, 1.78)
Boxing							
Gallacher et al. (2022),[34] retrospective cohort study	Former amateur athletes (non-boxing cohort members)	Wales	NR	NR	73 (5 dementia cases, 2 from Alzheimer's disease)	1037 (47 dementia cases, 26 from Alzheimer's disease)	Dementia: 1.73 (0.54, 5.56), Alzheimer's disease: 1.28 (0.26, 6.37)
Rugby union							
Russell et al. (2022),[35] retrospective cohort study	Former amateur athletes (general population)	Scotland	NR	Median 32 yr	412 (NR)	1236 (NR)	2.17 (1.26, 3.72)

NR, not reported.

Table 2: **Systematic review of past participation in contact sports and later dementia: Characteristics of included studies.**

differential; however, dropping the study from the meta-analysis did not substantially alter our conclusions.

Lastly, in analyses of the two cohorts of boxers (Fig. 4), both of whom competed on an amateur basis, former participants experienced a greater risk of both dementia (3.14 [1.72, 5.74]) and Alzheimer's disease (3.07 [1.01, 9.38]). There was a moderate level of heterogeneity across these two studies ($I^2 \leq 55\%$).

Discussion

In the present study, we quantitatively aggregated results from new analyses of a cohort of former amateur athletes with those from the extant literature. With the clear caveats that the evidence base is very modest in scale and confined to men, relative to general population comparison groups, we found elevated rates of dementia in former amateur participants from the contact sports of soccer, wrestling, and boxing but not American football. Amateurs in these analyses of American football athletes were denoted by former high school players and, in support of our observation for dementia, at autopsy, this group was found to have a markedly lower prevalence of chronic traumatic encephalopathy, a neurodegenerative disorder,[37] relative to erstwhile professionals and college players. The typically higher rates of neurodegenerative disorder in retired professionals may be ascribed to their greater exposure to head collisions resulting from more frequent training and competition relative to the amateur groups.

Another finding of the present meta-analysis was that, taken together, there was a general pattern of dementia risk despite the contrasting head impact profiles of the included contact sports. That is, concussions are most common in wrestling and boxing,[22,23] and result largely from person-on-person contact—in boxing, for

Study[citation]	Country	n/N Former athletes	n/N General population	Risk ratio (95% CI)
Dementia (overall)				
Mackay et al. 2019[8]	Scotland	180 / 7676	178 / 23028	3.87 (2.86 to 5.24)
Orhant et al 2022[9]	France	47 / 6114	13.9 / NR	3.38 (2.49 to 4.46)
Ueda et al. 2023[35]	Sweden	491 / 6007	2889 / 56168	1.62 (1.47 to 1.78)
Present study	Finland	44 / 248	120 / 1386	1.60 (1.11 to 2.30)
Pooled: I^2 = 94%, p < 0.01				**2.40 (1.48 to 3.90)**
Alzheimer's disease (overall)				
Mackay et al. 2019[8]	Scotland	64 / 7676	47 / 23028	5.07 (2.92 to 8.82)
Present study	Finland	35 / 248	71 / 1386	2.07 (1.23 to 3.46)
Pooled: I^2 = 81%, p = 0.02				**3.22 (1.34 to 7.75)**
Dementia (professional)				
Mackay et al. 2019[8]	Scotland	180 / 7676	178 / 23028	3.87 (2.86 to 5.24)
Orhant et. al 2022[9]	France	47 / 6114	13.9 / NR	3.38 (2.49 to 4.46)
Pooled: I^2 = 0%, p = 0.53				**3.61 (2.92 to 4.45)**
Dementia (professional and amateur)				
Ueda et al. 2023[35]	Sweden	491 / 6007	2889 / 56168	1.62 (1.47 to 1.78)
Pooled: I^2 = NA				NA
Dementia (amateur)				
Present study	Finland	44 / 248	120 / 1386	1.60 (1.11 to 2.30)
Pooled: I^2 = NA				NA

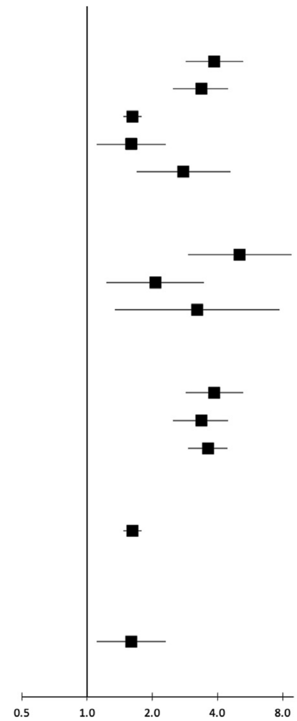

Fig. 2: **Risk ratios (95% confidence intervals) for the association of former participation in professional and amateur soccer with dementia and Alzheimer's disease: meta-analysis.** n = number of events, N = group size; NR = not reported; NA = not applicable.

instance, the primary objective is to render the opponent unconscious. In soccer, however, the insult is more likely to be sub-concussive and attributable to contact with equipment—the ball—when attempting to redirect it using the head. In within cohort analyses of former soccer players featured in the present meta-analysis,[8] those who occupied outfield positions in their careers and were therefore more likely to 'head' the ball, had higher rates of dementia at follow-up, including Alzheimer's, relative to goalkeepers who rarely do so.[38]

Most of the studies included in the present meta-analysis had a modest collection of confounding factors, however, in the analyses of the well-characterised Finnish cohort, controlling for an array of risk factors had little impact on the magnitude of the effects. This apparent independent influence of contact sports participation therefore raises the question of potential mechanisms. It is plausible that athleticism and neurodegenerative disorders share selected gene variants although empirical data are currently lacking. For those sports played in outdoor environments, it has been speculated that exposure to dementia-causing pesticides might raise disease risk,[39,40] though this would not apply to the indoor sports of boxing and wrestling where dementia risk was highest. Sport-specific explanations include, for soccer, the suggestion that heading produces an acute if temporary lowering of cognitive function,[41] while potentially more permanent structural changes to the brain are evident upon imaging.[42] Specific mechanisms of risk in boxing and American football (professionals) are less clear. That global participation in soccer—estimated at more than a quarter of a billion by its governing body[43]—is seemingly the highest of any sport, and programmes of wrestling are long-established in educational settings,[44] means that, if indeed causal, a link between a background in these activities and dementia may have public health significance.

The present study—analyses of new cohort data and a systematic review with meta-analysis—has its strengths, including being the first quantitative synthesis of dementia risk in former participants from a range of contact sports, one that incorporates new cohort study data, and provides some examination of amateur–professional risk differentials. It is not, however, without its limitations. First, all retrieved studies, the Finnish cohort included, exclusively sample men. While we can think of no reason for the results not

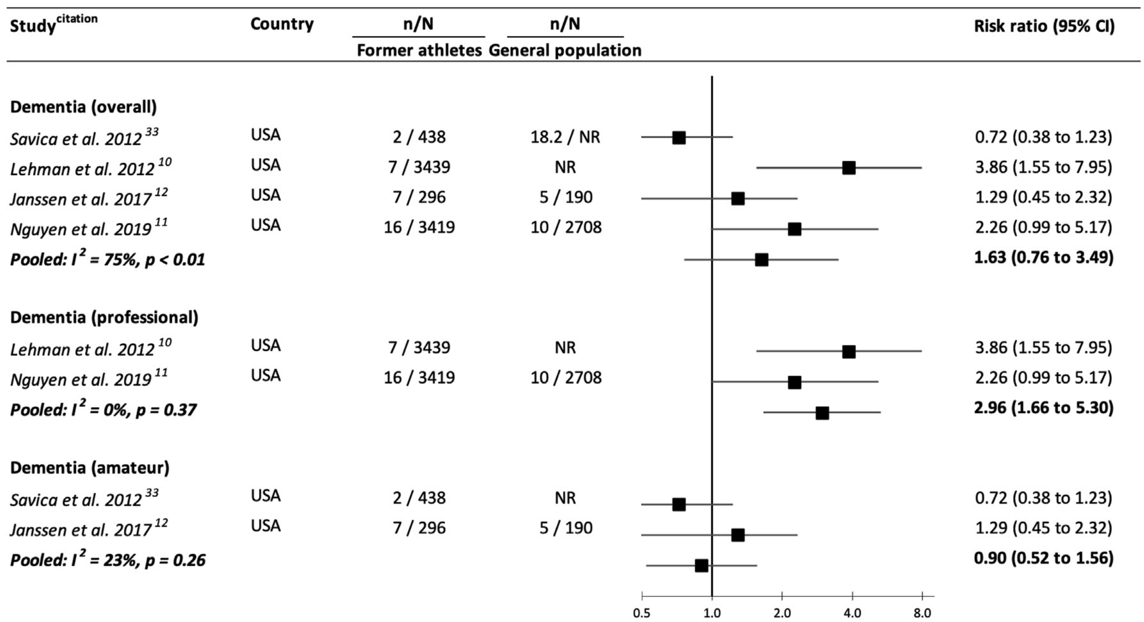

Fig. 3: **Risk ratios (95% confidence intervals) for the association of former participation in professional and amateur American football with dementia: meta-analysis**. n = number of events, N = group size; NR = not reported.

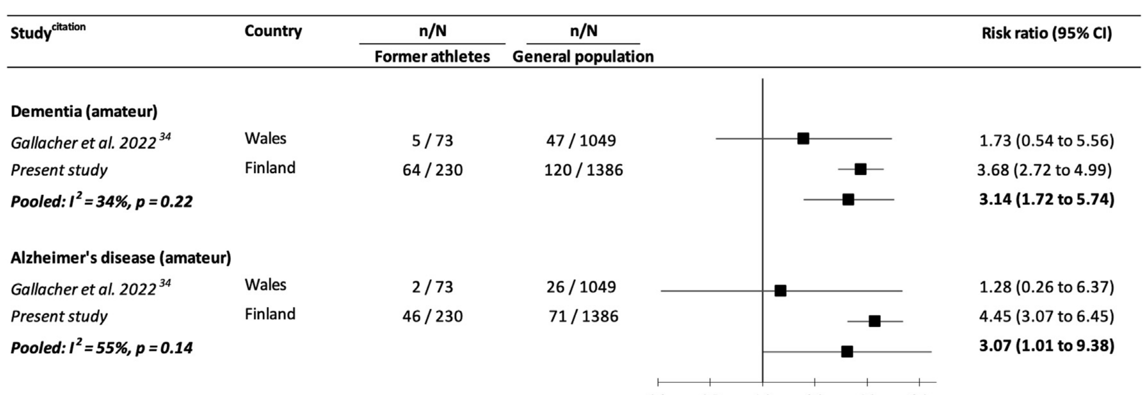

Fig. 4: **Risk ratios (95% confidence intervals) for the association of former participation in amateur boxing with dementia and Alzheimer's disease: meta-analysis**. n = number of events, N = group size.

applying to women given that other risk factors predict dementia equally well in sex-specific analyses,[45,46] this is an empirical question. Second, the findings of a meta-analysis are only as strong as the methodological quality of the studies it includes, and all data herein were observational. With conventional trials in this field being unviable ethically and perhaps logistically, an advance on current evidence may be the use of natural experiments. These could include the impact on dementia risk pre- and post-introduction of compulsory protective equipment such as change in the composition of the soccer ball from leather to plastic which would result in a lower weight in rain-soaked conditions (1986–present)—in many countries, soccer is a winter sport—or the introduction of head gear in amateur boxing (1984–2016). This quasi-experimental approach has been used elsewhere in dementia research by examining the role of mandated increases in school leaving age as a proxy for improved education.[47] Third, while using sports participation as a proxy for head impacts is the only approach used in the literature on exposure to head impacts and later risk of confirmed neurodegenerative events, other methods of data capture do exist, not least biomechanical devices which provide an objective measurement.[48] Inevitably, however, given the extended induction period for neurodegenerative disorders, it is likely to be decades until these studies yield useful data on risk factor associations.

Fourth, consideration of genetic liability in the context of confounding or effect modification in the collision sports–dementia relation was not possible owing to lack of available data in the Finnish cohort and the studies included in the systematic review. Apolipoprotein E (APOE) has been most consistently and strongly related to the occurrence of neurodegenerative disease, particularly Alzheimer's disease,[49] as have dozens of other variants.[50] Evidence linking APOE or other genetic factors with selection into specific sports, and associations with sports-acquired concussion[51] is, however, limited, and APOE does not appear to be an important moderator in the association between physical activity with brain health, broadly defined.[52] Lastly, in the Finnish cohort we were able to examine the relation of participation in contact sports with Alzheimer's disease but there were too few events in the non-Alzheimer group to examine effects for other dementia subtypes which include vascular dementia, dementia with Lewy Bodies, and Parkinson's disease dementia. Relatedly, of the neurodegenerative disorders, the highest magnitude of association may be for soccer and motor neuron disease (amyotrophic lateral sclerosis)[53] but, again, there were too few events to have confidence in the results of our survival analyses for this disorder.

In conclusion, based on a small collection of studies exclusively sampling men, former amateur participants in soccer, boxing, and wrestling experienced poorer brain health than the general population. Whether these findings are generalisable to the contact sports not featured, and to women, warrants examination.

Contributors

GDB generated the idea for the paper; formulated the plan for analyses of the cohort data; conducted the literature search for the systematic review; extracted results, prepared tables and figures; and drafted the manuscript. PF conducted the literature search for the systematic review; carried out the meta-analyses; prepared figures; and edited the manuscript. UMK and SJS initiated the Finnish cohort study; designed data collection; accessed and verified the cohort data; and edited the manuscript. CAV-H prepared figures and edited the manuscript. JK designed data collection in the Finnish cohort study; formulated the plan for analyses of cohort data; accessed, verified and analysed the Finnish cohort data; and edited the manuscript.

Data sharing statement

Bona fide interested parties should contact UMK and SJS for access to the Finnish cohort study data.

Declaration of interests

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2023.102056.

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