

Supplementary File

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eTable 1

Previous studies on the association between traumatic brain injury and dementia

Study	Setting	Study period	Study sample	Definition of TBI	Definition of dementia	Covariate definition and adjustment	Follow-up time	Main finding
Studies that found an association between traumatic brain injury and dementia								
Fann 2018* ¹	Denmark	1977–2013 (TBI) and 1999–2013 (dementia)	Total cohort, n=2,794,852 TBI, n=132,093, Dementia, n=126,734 Persons aged ≥50 years on January 1, 1995 were considered	Register based ICD-8/ICD-10	ICD-8/ICD-10 and/or at least one anti-dementia drug prescription	Age, sex, marital status, ICD-8/ICD-10 codes for medical comorbidities, neurological comorbidities, psychiatric comorbidities, drug-related abuse, alcohol-related abuse	Mean 9.9 years per patient	TBI versus no TBI increased the risk of dementia by a HR of 1.24–1.58 Mild TBI increased the risk of dementia by a HR of 1.17–1.46 Severe TBI increased the risk of dementia by a HR of 1.35–1.91
Nordström 2018* ²	Sweden	1964–2012 (TBI and dementia)	Cohort I, n=164,334 TBI and controls, Cohort II, n=136,233 dementia and controls; Cohort III, n=46,970 sibling pairs discordant for TBI Persons aged ≥50 years on December 31, 2005 were considered	Register based ICD-8/ICD-9/ICD-10	Register based ICD-8/ICD-9/ICD-10	Age, sex, civil status, education, early retirement pension, ICD-8/ICD-9/ICD-10 codes for medical comorbidities, alcohol intoxication and depression	Cohort I: mean 15.3 years, Cohort II: mean 18.8 years	TBI versus no TBI increased the risk of dementia by an OR of 1.71–1.89
Yaffe 2019* ³	U.S. Veterans (women)	2004–2015	n=109,140 females ≥55 years	Register based ICD-9	Register based ICD-9	ICD-9 for medical and psychiatric comorbidities, demographics (age, race/ethnicity, ZIP codes for socioeconomic classification)	Mean 4.0 years	TBI increased risk the risk of dementia by an sHR of 1.5 (95% CI 1.0–2.2)
Chu 2016* ⁴	Taiwan	2004–2005	n=12,931 TBI and n=51,724 controls	Register based ICD-9	Register based ICD-9	Age, sex, urbanization level, income, ICD-9 for comorbidities	Median 2.0 years	TBI increased the risk of dementia by a HR of 3.2 (95% CI 2.7–3.9)
Luukinen 2005* ⁵	Finland	1991–2000	n=152 persons ≥70 years	Hospitalization to university hospital	DSM-IV	Age, sex, education, diabetes, physical disability, alcohol use (self-reported), diabetes, BMI, MMSE, APOE ε4	9 years	TBI increased the risk of dementia by a HR of 2.6 (95% CI 1.3–5.5)
Sundström 2007* ⁶	Sweden	1988–1990, 1993–1995, 1998–2000	n=543	Self-reported and validated	DSM-IV	Age, sex, APOE ε4	At least 5 years	TBI without APOE ε4 did not increase the risk for dementia (OR 0.9, 95% CI 0.4–1.8), but TBI with APOE ε4 increased the risk for dementia (OR 5.2, 95% CI 2.0–14.0)
Luukinen 2008* ⁷	Finland	1991–1992	n=123 persons ≥70 years	Self-reported and validated	DSM-IV	Age, MMSE score, sex, educational status, APOE ε4	9 years	TBI without APOE ε4 did not increase the risk for dementia (OR 1.5, 95% CI 0.5–4.4), but TBI with APOE ε4 increased the risk for dementia (OR 2.7, 95% CI 1.02–7.2)
Abner 2014* ⁸	United States	1989–2004	n=649 ≥60 years	Self-reported	Post-mortem neuropathological diagnosis	Age, sex, education, APOE ε4, family history of dementia, hypertension and smoking (self-reported)	Not specified	TBI increased the risk for pathological diagnosis of AD by an OR of 1.5 in men but not in women

Rasmusson 1995** ⁹	United States	Not specified	n=68 persons with dementia and n=34 spouse controls	Self-reported by spouse informants	NINCDS-ADRDA Alzheimer's Criteria and neuropathological findings	Age, sex, education	Not specified	20% of familial and 43.5% of sporadic AD had premonitory history of TBI (OR 3.1). TBI had no effect of age of dementia onset
Nemetz 1999** ¹⁰	United States	1935–1984 (TBI)	n=1,283 persons with TBI	Manual review of medical records	Manual review of medical records	Age, sex	Until 1988	History of TBI shortened the time to AD diagnosis (median 10 years vs. 18 years from TBI, p=0.015). Calculated as the difference between observed and expected time of AD diagnosis.
Barnes 2014** ¹¹	United States	2000–2003 (baseline) and 2003–2012 (follow-up)	n=188,764 veterans ≥ years at baseline	Register based ICD-9	Register based ICD-9	Age, sex, ZIP code for education and income, ICD-9 codes for medical and psychiatric comorbidities	Mean 7.4 years	TBI increased the risk for dementia by a sHR of 1.8 (95% CI 1.6–2.1)
Gardner 2014** ¹²	California, US	2005–2011 2005–2006 (TBI)	n=51,799 persons with TBI ≥55 years	Register based ICD-9	Register based ICD-9	Age, sex, race, ICD-9 codes for medical comorbidities, trauma mechanism, trauma severity, health care use, ZIP code for socioeconomic classification	Median follow-up 6 years No censoring at death	TBI increased the risk of dementia by a HR of 1.3 (95% CI 1.2–1.3) Mild TBI increased the risk for dementia in persons ≥65 years (HR 1.5, 95% CI 1.3–1.6) but not in persons 55–64 years) Moderate-to-severe TBI increased the risk for TBI in all persons ≥55 years (for those 55–64 years HR 1.7, 95% CI 1.4–2.1, for those 65–74 years HR 1.5, 95% CI 1.3–1.6)
Nordström 2014** ¹³	Sweden	1969–1986	n=811,622 men	Register based ICD-8/ICD-9/ICD-10	Register based ICD-8/ICD-9/ICD-10	Age, place and year of conscription, weight, height, knee strength, blood pressure, cognitive function score, education, income, heritability (dementia and TBI in parents), ICD-8/ICD-9/ICD-10 diagnoses during follow up (including alcohol intoxication, drug intoxication, depression, stroke	Median 33 years	One mild TBI increased the risk for dementia by a HR of 1.5 (95% CI 1.1–2.0). Specifically, one mild TBI increased the risk for non-AD dementia (HR 1.7, 95% CI 1.2–2.3) but not for AD (HR 1.0, 95% CI 0.5–2.0) One severe TBI increased the risk for dementia by a HR of 2.3 (95% CI 1.5–3.6). Specifically, one severe TBI increased the risk for non-AD dementia (HR 2.6, 95% CI 1.6–4.1) but not for AD (HR 0.7, 95% CI 0.1–5.2)
Wang 2012** ¹⁴	Taiwan	2000–2004 (TBI)	n=44,925 persons with TBI and n=224,625 controls without TBI	Register based ICD-9	Register based ICD-9	Age, sex, area of living, ICD-9 codes for comorbidities	5-year follow-up	TBI increased the risk of dementia by a HR of 1.7 (95% CI 1.6–1.8)
Schneider 2021 ¹⁵	United States	1987–1989	n=3440 persons with head injury and n=10,936 persons with no head injury	Self-reported, hospitalization data (ICD-9/ICD-10)	Cognitive assessments, telephone interview, hospitalization ICD-9 codes, death certificate	Age, race, education, family income, physical activity index, cigarette smoking, alcohol consumption, hypertension, diabetes, coronary heart disease, apolipoprotein E, depression, post-traumatic stress disorder	Median 25 years	Head injury increased the risk of dementia by a HR of 1.44 (95% CI 1.32–1.57). In a model adjusting for competing risk, HR was 1.72 (95% CI 1.57–1.89). The risk was higher among women than among men.
Tolppanen 2017 ¹⁶	Finland	2005–2011 (diagnosis of AD)	n=70,719 persons with AD and 282,862 controls	Register based ICD-9/ICD-10	Clinically verified diagnosis of AD	Age, sex, psychotropic and epileptic drugs (ATC codes), comorbidities and substance	Not stated	TBI versus no TBI increased the risk of AD by an OR of 1.23 (95% CI 1.18–1.29)

		1972–2011 (TBI)				abuse (ATC codes and ICD-10), socioeconomic status		Mild TBI increased the risk of AD by an OR of 1.19 (95% CI 1.12–1.25) Severe TBI increased the risk of AD by an OR of 1.36 (95% CI 1.25–1.48)
Barnes 2018 ¹⁷	U.S. Veterans (91% men)	2001–2014 (TBI)	n=178,779 persons with TBI and 178,779 controls	Clinical evaluation and ICD-9	Register based ICD-9	ICD-9 for medical comorbidities, psychiatric disorders and substance abuse, self-reported demographic information (age, sex, race/ethnicity)	Not reported	Mild TBI without loss of consciousness increased the risk of dementia by an HR of 2.4 (95% CI 2.1–2.7) Mild TBI with loss of consciousness increased the risk of dementia by an HR of 2.5 (95% CI 2.3–2.8) Moderate-to-severe TBI increased the risk of dementia by an HR of 3.8 (95% CI 3.6–3.9)
Redelmeier 2019 ¹⁸	Ontario, Canada	1993–2013 (TBI)	n=28,815 persons ≥66 years with concussion	Register based ICD-9	Register based ICD-9	Age, sex, socioeconomic quintile, home location, Ontario Drug Benefit program database for use of cardiovascular medications, neuropsychiatric medications, and miscellaneous medications	Mean 3.9 years	One in six persons with concussion developed dementia during a mean follow-up of 3.9 years
Lee 2013 ¹⁹	Taiwan	2005–2009	n=28551 persons with mild TBI	Register based ICD-9	ICD-9 and anti-dementia drug prescription or a "catastrophic illness certificate" application	Age, gender, urbanization level, socioeconomic status, ICD-9 codes for medical comorbidities	1 year	Mild TBI increased risk for dementia by a HR of 3.3 (95% CI 2.7–3.9). Median time from mild TBI to dementia was 1.0 years (95% CI 0.8–1.2)
Raj 2017 ²⁰	Finland	1987–2014	n=19,936 persons with moderate-to-severe TBI and n=20,7033 persons with mild TBI	Register based ICD-9/ICD-10	Register based ICD-9/ICD-10	Age, sex, socioeconomic status, education level	Mean 11 years	Moderate-to-severe TBI increased the risk of dementia compared to mild TBI with a HR of 1.9 (95% CI 1.6–2.2)
Guo 2000 ²¹	United States, Canada, and Germany	1991–1996	n=2,233 persons with AD and unaffected spouse(s) controls	Informant questionnaire	NINCDS-ADRDA Alzheimer's Criteria	Age and sex	NA	Head injury with loss of consciousness increased the risk of dementia by an OR of 9.9 (95% CI 6.5–15.1) Head injury without loss of consciousness increased the risk of dementia by an OR of 3.1 (95% CI 2.3–4.0)
Studies that did not find any association between traumatic brain injury and dementia								
Mehta 1999 ^{*22}	Netherlands (Rotterdam)	1990–1993	n=6,645 persons ≥55 years	Self-reported questionnaire	Dementia diagnosis according to the DSM-III-R criteria AD diagnosis according to NINCDS-ADRDA Alzheimer's Criteria	Age, sex, education	Mean 2.1 years	History of head trauma did not significantly increase the risk of (loss of consciousness, multiple TBIs, duration of loss of consciousness did not affect)

Dams-O'Connor 2013 ²³	United States	1994–2010	n=3,466 persons ≥65 years	Self-reported questionnaire	Dementia diagnosis according to the DSM-IV criteria AD diagnosis according to NINCDS-ADRDA Alzheimer's Criteria	Age, sex, education, APOE ε4	Mean 7.4 years	History of TBI with loss of consciousness did not significantly increase risk for dementia independent of age at the time of head injury
Crane 2016 ²⁴	United States	1994–2004	Cohort I, n=3,666 Cohort II, n=2,689	Self-reported questionnaire	Dementia diagnosis according to the DSM-IV criteria AD diagnosis according to NINCDS-ADRDA Alzheimer's Criteria Clinical, neuropsychological and cognitive testing	Age, sex, education, APOE ε4	Cohort I: Mean 7.8 years Cohort II: Mean 5.5 years	History of TBI with loss of consciousness did not significantly increase risk for dementia

*New added evidence included in 2020 Lancet Commission on dementia prevention, intervention and care.

**Studies included as original evidence used by 2020 Lancet Commission on dementia prevention, intervention and care stemming from a meta-analysis by Huang and colleagues ²⁵

AD=Alzheimer's Disease, BMI=Body Mass Index, CI=Confidence Interval, HR=Hazards Ratio, MMSE=Mini Mental State Examination, OR=Odds Ratio, sHR=sub-Hazard Ratio, NINCDS-ADRDA=National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association, DSM-=Diagnostic and Statistical Manual of Mental Disorders

eMethods

Educational status definition

Educational status was classified as low, middle and high. Educational status was calculated by dividing years of formal education into tertiles within each birth cohort, separately for men and women. This in order to account for the steep increase in rise in schooling during the 20th century.²⁶

Leisure time physical activity definition

Leisure time physical activity was defined as follows:

1. Sedentary: In my leisure time I read, watch TV, and work in the household with tasks which do not make me move much and which do not physically tax me.
2. Light: In my spare time I walk, cycle or exercise otherwise at least 4 hours per week. This includes walking, fishing and hunting, light gardening etc. but excludes travel to work.
3. Moderate: In my spare time I exercise to maintain my physical condition, e.g. running, jogging, skiing, gymnastics, swimming, playing ball games or I do heavy gardening or the like for at least 3 hours per week.
4. Intensive: In my spare time I regularly exercise competitive-wise several times a week running, orienteering, skiing, swimming, playing ball games or other heavy sports.

The classification has shown good criterion validity against morbidity and mortality and moderate correlation against accelerometer counts among the working-age population.²⁷ The categories moderate activity and 4 (intensive activity were combined due to the low number of participants in the intensive group (<2% of all).

Alcohol consumption definition

Alcohol consumption was assessed with structured questionnaires regarding the average amount of alcohol they had consumed the week prior to the survey. Average alcohol intake (grams per day) was calculated as the sum of the daily number of drinks multiplied by the average alcohol content per type of alcoholic beverage.

The amount of ethanol in different beverages was quantitated based on defined portion sizes as follows: regular beer 12 grams (1/3 L), strong beer 15.5 grams (1/3 L), long drink 15.5 grams (1/3 L), spirit 12 grams (4 cL), wine 12 grams (12 cL) and cider 12 grams (1/3 L). A dose of 12 grams of pure ethanol was considered as one standard drink.

The data on alcohol consumption was subsequently used to categorize the population by gender and drinking habits as follows: i) participants who reported no current alcohol consumption were referred to as non-drinkers, ii) light drinkers consumed between 1–13 drinks (men) or 1–6 drinks (women), iii) moderate drinkers consumed 14–23 drinks (men) or 7–15 drinks (women) and iv) heavy drinkers consumed more than 23 drinks (men) or more than 15 drinks (women) per week.²⁸

For the analyses, moderate and heavy drinkers were combined into one category due to the low number of participants in the heavy drinking group (<5%).

Smoking definition

Current smoker (including those that stopped less than 6 months ago), former smoker (stopped more than 6 months ago), and non-smoker. Current regular smokers were divided current smokers based upon number of cigarettes used to ≤ 15 cigarettes per day (light to moderate smokers) and > 15 cigarettes per day (heavy smokers).²⁹ The non-smoker group may contain occasional smokers.

References for eTable 1 and eMethods

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eTable 2

Baseline characteristics for the whole cohort

Variables	All participants (n=32,385)	Men (n=15,106)	Women (n=17,279)
Age at baseline, median (IQR)	46 (36, 55)	46 (36, 56)	45 (35, 55)
Sex			
Female	17,279 (53%)	NA	17,279 (100%)
Male	15,106 (47%)	15,106 (100%)	NA
Educational status*			
Low	10,206 (32%)	4,663 (31%)	5,543 (32%)
Average	10,599 (33%)	4,926 (33%)	5,673 (33%)
High	11,273 (35%)	5,367 (36%)	5,906 (34%)
Alcohol consumption†			
Non-drinker	11,120 (35%)	3,925 (27%)	7,195 (42%)
Light drinker	14,928 (47%)	7,843 (53%)	7,085 (42%)
Moderate to heavy drinker	5,683 (18%)	2,981 (20%)	2,712 (16%)
Smoking‡			
Non-smoker	16,919 (53%)	6,322 (42%)	10,597 (62%)
Former smoker	6,897 (21%)	3,920 (26%)	2,977 (17%)
Current, ≤15 cigarettes/day	5,048 (16%)	2,333 (16%)	2,716 (16%)
Current, >15 cigarettes/day	3,359 (10%)	2,449 (16%)	910 (5%)
Leisure time physical activity¶			
Sedentary	7,302 (23%)	3,359 (23%)	3,943 (23%)
Light	16,834 (52%)	7,526 (50%)	9,308 (54%)
Moderate to intense	7,973 (25%)	4,103 (27%)	3,870 (23%)
Hypertension§	14,669 (45%)	7,337 (48%)	7,332 (43%)
Median time at risk per participant, years	15.8	15.9	15.9

Abbreviations: IQR=interquartile range.

*307 missing values (0.9%), †653 missing values (2.0%), ‡162 missing values (0.5%), ¶276 missing values (0.9%), §85 missing values (0.3%)

eTable 3

Baseline characteristics for participants with a history of minor and major traumatic brain injury before and after FINRISK participation

Variable	Minor TBI before entry (n=238)	Minor TBI after entry (n=168)	p-value	Major TBI before entry (n=127)	Major TBI after entry (n=161)	p-value
Age at baseline , median (IQR)	43 (32, 53)	47 (39, 55)	0.007	52 (41, 59)	55 (45, 61)	0.053
Age at TBI , median (IQR)	24 (16, 39)	56 (47, 67)	<0.001	40 (23, 50)	64 (55, 74)	<0.001
Age at dementia , median (IQR)	76 (69, 80)	78 (72, 84)	0.807	73 (66, 77)	73 (69, 80)	0.651
Sex						
Female	99 (42%)	69 (41%)	0.916	35 (28%)	47 (29%)	0.760
Male	139 (58%)	99 (59%)		92 (72%)	114 (71%)	
Educational status						
Low	74 (31%)	63 (38%)	0.227	53 (43%)	57 (37%)	0.535
Average	88 (37%)	49 (30%)		36 (29%)	49 (31%)	
High	75 (32%)	53 (32%)		35 (28%)	51 (32%)	
Alcohol consumption						
Non-drinker	87 (38%)	69 (43%)	0.570	52 (42%)	49 (31%)	0.178
Light drinker	104 (44%)	65 (40%)		47 (38%)	67 (43%)	
Moderate to heavy drinker	41 (18%)	28 (17%)		25 (20%)	40 (26%)	
Smoking						
Non-smoker	114 (48%)	86 (52%)	0.594	39 (31%)	71 (44%)	0.113
Former smoker	51 (21%)	27 (16%)		26 (21%)	30 (19%)	
Current, ≤15 cigarettes/day	42 (18%)	30 (18%)		32 (26%)	27 (17%)	
Current, >15 cigarettes/day	30 (13%)	24 (14%)		27 (22%)	32 (20%)	
Leisure time physical activity						
Sedentary	54 (23%)	46 (28%)	0.107	41 (34%)	32 (20%)	0.035
Light	110 (46%)	83 (50%)		62 (50%)	99 (62%)	
Moderate to intense	74 (31%)	36 (22%)		19 (16%)	29 (18%)	
Hypertension	108 (45%)	73 (43%)	0.701	55 (43%)	95 (59%)	0.008
Median time at risk per participant , years	15.8	20.7		15.7	19.5	

Abbreviations: IQR=interquartile range, TBI=traumatic brain injury.

eTable 4

Age at time of death and time of dementia stratified by covariates

Variables	Median age at time of death (IQR)	Median age at time of dementia (IQR)
	Total N = 3,339	Total N = 1,010
All	69.3 (61.5–76.6)	75.4 (70.2–79.5)
No TBI	69.3 (61.6–76.6)	75.5 (70.2–79.5)
Minor TBI	71.4 (58.9–77.7)	76.4 (72.9–82.1)
Major TBI	70.6 (60.8–76.1)	72.7 (67.1–78.1)
Sex		
Female	71.1 (62.7–78.3)	74.7 (69.5–79.3)
Male	68.3 (60.7–75.4)	75.7 (70.5–79.8)
Educational status		
Low	68.1 (60.7–75.2)	74.3 (70.0–78.9)
Average	69.0 (60.9–76.6)	75.7 (70.0–79.8)
High	70.9 (63.0–77.9)	76.0 (70.8–79.6)
Alcohol consumption		
Non-drinker	71.4 (63.9–78.1)	75.7 (70.6–79.8)
Light drinker	69.5 (61.6–76.7)	75.5 (70.2–79.7)
Moderate to heavy drinker	65.2 (57.6–72.6)	72.5 (66.6–77.5)
Smoking		
Non-smoker	72.2 (63.4–79.1)	76.1 (71.0–80.1)
Former smoker	71.4 (64.7–77.4)	75.4 (69.7–79.2)
Current, ≤15 cigarettes/day	66.2 (57.8–73.6)	73.3 (68.0–77.6)
Current, >15 cigarettes/day	65.4 (58.3–71.7)	70.6 (64.8–77.4)
Leisure time physical activity		
Sedentary	67.1 (59.9–74.8)	73.2 (67.9–78.5)
Light	70.5 (62.9–77.3)	75.9 (71.0–80.0)
Moderate to intense	68.3 (57.8–76.3)	75.2 (69.2–79.5)
Hypertension		
No	66.0 (57.6–74.5)	74.4 (69.4–79.0)
Yes	70.5 (63.5–77.4)	75.6 (70.5–79.8)

Abbreviations: IQR=interquartile range.

eTable 5

Baseline characteristics for participants developing dementia according to history of traumatic brain injury

Variables	Dementia cases with no history of TBI (n=940)	Dementia cases with a history of minor TBI (n=9)	Dementia cases with a history of major TBI (n=27)
Age at baseline, median (IQR)	60 (55–62)	61 (59–64)	59 (54–61)
Age at time of TBI, median (IQR)	NA	59 (47–69)	56 (46–69)
Age at time of dementia, median (IQR)	75 (70–79)	76 (73–82)	73 (67–78)
Sex			
Female	524 (56%)	3 (33%)	8 (30%)
Male	416 (44%)	6 (67%)	19 (70%)
Educational status			
Low	301 (32%)	6 (67%)	5 (19%)
Average	285 (31%)	1 (11%)	6 (23%)
High	340 (37%)	2 (22%)	15 (58%)
Alcohol consumption			
Non-drinker	455 (50%)	5 (56%)	13 (52%)
Light drinker	353 (38%)	4 (44%)	8 (32%)
Moderate to heavy drinker	113 (12%)	0 (0%)	4 (16%)
Smoking			
Non-smoker	569 (61%)	7 (78%)	10 (38%)
Former smoker	201 (22%)	0 (0%)	9 (35%)
Current, ≤15 cigarettes/day	96 (10%)	2 (22%)	2 (8%)
Current, >15 cigarettes/day	66 (7%)	0 (0%)	5 (19%)
Leisure time physical activity			
Sedentary	217 (24%)	3 (33%)	9 (36%)
Light	589 (64%)	6 (67%)	11 (44%)
Moderate to intense	117 (12%)	0 (0%)	5 (20%)
Hypertension	629 (67%)	6 (67%)	16 (59%)

Abbreviations: IQR=interquartile range.

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eTable 6

Unadjusted incidence of dementia per 10,000 person-years for participants with no traumatic brain injury and minor or major traumatic brain injury

Variable	Unadjusted incidence of dementia per 10,000 person-years (95% CI)		
	No TBI (n=31,125)	Minor TBI (n=406)	Major TBI (n=288)
25–39 years	0.5 (0.2–0.9)	NA*	10.3 (1.4–72.9)
40–49 years	6.3 (5.1–7.8)	NA*	36.3 (13.6–96.8)
50–59 years	23.1 (26.2–32.5)	13.6 (3.4–54.5)	70.0 (37.7–130.2)
60–64 years	86.0 (78.6–94.2)	91.5 (43.6–191.8)	109.5 (62.2–192.8)

Abbreviations: CI=confidence intervals, TBI=traumatic brain injury.

*No dementia cases

eTable 7

Cox proportional hazards models showing the effects of individual risk factors on the association between traumatic brain injury and risk of dementia

Hazard ratio (95% confidence intervals)						
Category	No risk factors	Educational level	Smoking	Alcohol consumption	Physical activity	Hypertension
No TBI	1.0	1.0	1.0	1.0	1.0	1.0
Minor TBI	0.67 (0.35–1.29)	0.65 (0.34–1.26)	0.67 (0.35–1.29)	0.66 (0.34–1.27)	0.66 (0.34–1.27)	0.67 (0.35–1.29)
Major TBI	1.51 (1.03–2.22)	1.48 (1.00–2.18)	1.47 (0.99–2.18)	1.39 (0.93–2.07)	1.41 (0.94–2.10)	1.51 (1.03–2.21)

*all models adjusted for sex, year of FINRISK participation

Education level categories are low, middle and high.

Smoking categories are non-smoker, former smoker, current smoker ≤ 15 cigarettes per day, current smoker > 15 cigarettes per day.

Alcohol consumption are categorized according to gender and number of drinks per day (*please see "Alcohol consumption definition"*)

Leisure time activity categories are sedentary, light and moderate to intense.

Hypertension categories are no hypertension and hypertension.

eTable 8

Results of the sensitivity analysis that included only participants suffering from traumatic brain injury after FINRISK participation

Variable	HR (95% CI)	p-value
Partially adjusted model		
History of TBI		
No TBI	1.0	
Minor TBI	0.41 (0.14–1.10)	0.077
Major TBI	0.75 (0.40–1.41)	0.374
Sex		
Male	1.0	
Female	0.97 (0.85–1.10)	0.625
Fully adjusted		
History of TBI		
No TBI	1.0	
Minor TBI	0.40 (0.15–1.08)	0.070
Major TBI	0.68 (0.35–1.13)	0.250
Sex		
Male	1.0	
Female	0.89 (0.77–1.03)	0.111
Education status		
Low	1.0	
Middle	0.80 (0.67–0.94)	0.009
High	0.79 (0.67–0.93)	0.005
Smoking		
Non-smoker	1.0	
Former smoker	0.97 (0.81–1.16)	0.728
Current, ≤15 cigarettes/day	1.21 (0.97–1.52)	0.096
Current, >15 cigarettes/day	0.95 (0.72–1.26)	0.724
Alcohol consumption		
Non-drinker	1.27 (1.10–1.48)	0.001
Light drinker	1.0	
Moderate to heavy drinker	1.22 (0.97–1.52)	0.083
Leisure time physical activity		
Sedentary	1.0	
Light	0.86 (0.73–1.01)	0.060
Moderate to intense	0.74 (0.58–0.93)	0.010
Hypertension		
	1.01 (0.88–1.17)	0.853

Both models adjusted for adjusted for year of FINRISK study participation

Abbreviations: CI=confidence interval, HR=hazards ratio

eTable 9

Results of the sensitivity analysis that used the competing risks model

Variable	sHR (95% CI)	p-value
History of TBI		
No TBI	1.0	
Minor TBI	0.64 (0.33–1.23)	0.178
Major TBI	1.18 (0.77–1.83)	0.446
Education status		
Low	1.0	
Middle	0.82 (0.70–0.97)	0.020
High	0.85 (0.73–1.00)	0.053
Smoking		
Non-smoker	1.0	
Former smoker	0.92 (0.78–1.09)	0.336
Current, ≤15 cigarettes/day	0.95 (0.76–1.19)	0.660
Current, >15 cigarettes/day	0.63 (0.48–0.83)	0.001
Alcohol consumption		
Non-drinker	1.24 (1.08–1.44)	0.003
Light drinker	1.0	
Moderate to heavy drinker	1.04 (0.84–1.29)	0.725
Leisure time physical activity		
Sedentary	1.0	
Light	0.92 (0.78–1.07)	0.278
Moderate to intense	0.80 (0.64–1.01)	0.063
Hypertension	1.02 (0.88–1.17)	0.823

Abbreviations: CI=confidence interval, sHR=subhazard ratio
 Model also adjusted for year of FINRISK participation

eTable 10

Characteristics of participants included in the nested case–control analysis

Variables	Controls (n=3,952)	Cases (n=988)
Age at entry , median (IQR)	60 (56, 63)	60 (56, 62)
Age at exit , median (IQR)	80 (76, 84)	76 (70, 80)
Minor TBI	53 (1.4%)	9 (0.9%)
Major TBI	81 (2.1%)	27 (2.8%)
Sex		
Female	2,172 (55%)	543 (55%)
Male	1,780 (45%)	445 (45%)
Educational status*		
Low	1,094 (28%)	317 (32%)
Average	1,205 (31%)	290 (30%)
High	1,613 (41%)	367 (38%)
Alcohol consumption†		
Non-drinker	1,708 (45%)	484 (50%)
Light drinker	1,706 (44%)	370 (38%)
Moderate to heavy drinker	428 (11%)	113 (12%)
Smoking‡		
Non-smoker	2,391 (61%)	596 (61%)
Former smoker	914 (23%)	213 (22%)
Current, ≤15 cigarettes/day	355 (9%)	99 (10%)
Current, >15 cigarettes/day	267 (7%)	70 (7%)
Leisure time physical activity¶		
Sedentary	744 (19%)	231 (24%)
Light	2,500 (64%)	615 (63%)
Moderate to intense	650 (17%)	122 (13%)
Hypertension§	2,632 (67%)	664 (67%)

Abbreviations: IQR=interquartile range.

*54 missing values, †131 missing values, ‡35 missing values, ¶78 missing values, §7 missing values

eTable 11

Results of the nested case–control conditional logistic regression analysis

Variable	OR (95% CI)	p-value
History of TBI		
No TBI	1.0	
Minor TBI	0.72 (0.35–1.48)	0.372
Major TBI	1.20 (0.74–1.96)	0.465
Education status		
Low	1.0	
Middle	0.87 (0.72–1.05)	0.139
High	0.84 (0.70–1.01)	0.070
Smoking		
Non-smoker	1.0	
Former smoker	0.96 (0.78–1.17)	0.671
Current, ≤15 cigarettes/day	1.16 (0.89–1.50)	0.272
Current, >15 cigarettes/day	0.98 (0.72–1.34)	0.912
Alcohol consumption		
Non-drinker	1.25 (1.06–1.47)	0.008
Light drinker	1.0	
Moderate to heavy drinker	1.21 (0.94–1.55)	0.139
Leisure time physical activity		
Sedentary	1.0	
Light	0.82 (0.69–0.99)	0.037
Moderate to intense	0.69 (0.53–0.89)	0.004
Hypertension	0.99 (0.85–1.17)	0.950

Abbreviations: CI=confidence interval, OR=odds ratio

eTable 12

Results of the nested case–control conditional logistic regression analysis after excluding controls who later developed dementia

The `sttocc` function in Stata generates a nested case–control study data by sampling controls from the risk sets. For each case (dementia), the controls (non-dementia) are chosen randomly from participants who are at risk at the failure time of the case. That is, the resulting case–control sample is matched with respect to analysis time—the time scale used to compute risk sets (Langholz, B., and D. C. Thomas. 1990. *Nested case-control and case-cohort methods of sampling from a cohort: A critical comparison*. American Journal of Epidemiology 131: 169–176). Thus, the controls are non-demented at the time of matching but can potentially develop dementia afterwards. Of the 3,952 controls, 433 developed dementia later on. Thus, we conducted another analysis excluding these 433 controls that developed dementia later on, leaving 3,519 controls (non-dementia) and 988 cases (dementia). The results are shown below:

Variable	OR (95% CI)	p-value
History of TBI		
No TBI	1.0	
Minor TBI	0.73 (0.35–1.49)	0.384
Major TBI	1.18 (0.71–1.94)	0.523
Education status		
Low	1.0	
Middle	0.88 (0.73–1.07)	0.198
High	0.82 (0.68–0.99)	0.039
Smoking		
Non-smoker	1.0	
Former smoker	0.96 (0.79–1.18)	0.731
Current, ≤15 cigarettes/day	1.14 (0.88–1.48)	0.321
Current, >15 cigarettes/day	0.95 (0.69–1.30)	0.741
Alcohol consumption		
Non-drinker	1.29 (1.09–1.52)	0.003
Light drinker	1.0	
Moderate to heavy drinker	1.21 (0.94–1.55)	0.143
Leisure time physical activity		
Sedentary	1.0	
Light	0.83 (0.69–0.99)	0.043
Moderate to intense	0.69 (0.53–0.89)	0.005
Hypertension	1.04 (0.89–1.22)	0.616

Abbreviations: CI=confidence interval, OR=odds ratio

eTable 13

Characteristics of participants included in the matched exposed–nonexposed analysis

Variables	Minor TBI		Major TBI	
	Exposed (n=405)	Non-exposed (n=809)	Exposed (n=280)	Non-exposed (n=584)
Age at baseline, median (IQR)	45 (35, 54)	45 (35, 55)	53 (44, 60)	47 (37, 57)
Age at TBI, median (IQR)	40 (21, 54)	NA	54 (40, 67)	NA
Age at dementia, median (IQR)	76 (73, 82)	77 (72, 81)	72 (66, 76)	77 (72, 79)
Age at death, median (IQR)	71 (59, 78)	68 (62, 76)	71 (61, 76)	72 (64, 79)
Sex				
Female	168 (42%)	341 (42%)	80 (29%)	169 (29%)
Male	237 (58%)	468 (58%)	200 (71%)	415 (71%)
Educational status*				
Low	137 (34%)	281 (35%)	108 (39%)	222 (38%)
Average	137 (34%)	270 (34%)	83 (30%)	174 (31%)
High	127 (32%)	252 (31%)	86 (31%)	183 (31%)
Alcohol consumption†				
Non-drinker	156 (40%)	318 (40%)	97 (36%)	201 (35%)
Light drinker	168 (43%)	336 (43%)	113 (41%)	237 (41%)
Moderate to heavy drinker	69 (17%)	135 (17%)	64 (23%)	136 (24%)
Smoking‡				
Non-smoker	200 (50%)	404 (50%)	110 (40%)	232 (40%)
Former smoker	78 (19%)	158 (20%)	54 (19%)	121 (20%)
Current, ≤15 cigarettes/day	72 (18%)	139 (17%)	57 (20%)	114 (20%)
Current, >15 cigarettes/day	54 (13%)	106 (13%)	58 (21%)	117 (20%)
Leisure time physical activity¶				
Sedentary	100 (25%)	199 (25%)	72 (26%)	145 (25%)
Light	192 (48%)	387 (48%)	158 (57%)	333 (58%)
Moderate to intense	110 (27%)	219 (27%)	47 (17%)	100 (17%)
Hypertension§	181 (45%)	365 (45%)	148 (53%)	317 (54%)

Abbreviations: IQR=interquartile range, TBI=traumatic brain injury

*18 missing values, †48 missing values, ‡5 missing values, ¶16 missing values

eTable 14

Risk of dementia based on the matched exposed–nonexposed Cox proportional hazards analyses

Variable	HR (95% CI)	p-value
History of TBI		
No TBI	1.0	
Minor TBI	0.78 (0.36–1.71)	0.535
History of TBI		
No TBI	1.0	
Major TBI	1.66 (0.90–3.07)	0.106

Abbreviations: CI=confidence interval, HR=hazards ratio