Prevalence, associated factors, mood and cognitive outcomes of traumatic brain injury in later life: The Health In Men Study (HIMS)

Osvaldo P. Almeida, MD, PhD, FRANZCP^{1,2,3}

Graeme J. Hankey, MBBS, MD, FRACP, FRCP^{4,5}

Bu B. Yeap, MBBS, PhD, FRACP^{4,6}

Jonathan Golledge, MA, MB, BChir, MChir, FRCS, FRACS^{7,8}

Leon Flicker, MBBS, PhD, FRACP^{2,4,9}

¹ School of Psychiatry & Clinical Neurosciences, University of Western Australia, Perth, Australia

² WA Centre for Health & Ageing, Centre for Medical Research, Perth, Australia

³ Department of Psychiatry, Royal Perth Hospital, Perth, Australia

⁴ School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

⁵ Department of Neurology, Sir Charles Gairdner Hospital, Perth, Australia

⁶ Department of Endocrinology and Diabetes, Fremantle and Fiona Stanley Hospitals, Perth, Australia

⁷ Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville, Australia

⁸ Department of Vascular and Endovascular Surgery, The Townsville Hospital, Townsville, Australia

⁹ Department of Geriatric Medicine, Royal Perth Hospital, Perth, Australia

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Key points:

- 17% of community-dwelling men older than 70 years have experienced a clinically significant traumatic brain injury in the past.
- History of traumatic brain injury is associated with increased risk of depression and cognitive impairment in later life.

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Correspondence

Prof. Osvaldo P. Almeida, School of Psychiatry & Clinical Neurosciences (M573), University of Western Australia, 35 Stirling Highway, Crawley, Perth, WA 6009, Australia. Email: osvaldo.almeida@uwa.edu.au.

ABSTRACT

Background: The incidence of traumatic brain injury (TBI) is rising, as are its neuropsychiatric complications. This study aims to determine (1) the prevalence of TBI, (2) the association between history of past TBI and sociodemographic, lifestyle and clinical factors, (3) the risk of depression and cognitive impairment in later life associated with exposure to TBI.

Methods: Cross-sectional study of a community-derived sample of 5,486 Australian men aged 70-89 years. Information on TBI was retrieved from the Western Australian Data Linkage System (WADLS) and via self-report. We used the WADLS and self-report to ascertain history of past depression, and the Geriatric Depression Scale 15-items to assess current clinically significant symptoms of depression, defined by score ≥ 7 . We defined cognitive impairment by a Mini-Mental State Examination score < 24 or a WADLS diagnosis of dementia.

Results: 953 men had history of TBI (17.4%). Factors associated with TBI included coronary heart disease, stroke, poor self-perceived physical health and falls. TBI increased the odds ratio of past (OR=1.55, 95%CI=1.21,1.99) and current depression (OR=1.77, 95%CI=1.36,2.32), as well as of cognitive impairment (OR=1.23, 95%CI=1.00,1.51). The population fractions of depression and cognitive impairment attributable to TBI were 6.9% (95%CI=3.3%,10.3%) and 3.4% (95%CI=0.0%,6.9%).

Conclusions: History of TBI is common in older men, and is associated with increased risk of depression and cognitive impairment. If this association is truly causal, then the effective reduction of events leading to TBI (e.g., motor vehicle accidents and falls) may also decrease the prevalence of depression and cognitive impairment in later life.

INTRODUCTION

Concurrent with the ageing of the world's population, the incidence of traumatic brain injury (TBI) has been rising, particularly in older people (Roozenbeek *et al.*, 2013). Currently available estimates of the incidence of TBI in Europe, Australia and Asia indicate rates of about 250 per 100,000 (Tagliaferri *et al.*, 2006), but rates can be at least 3 times higher if less severe cases of TBI are also considered (Feigin *et al.*, 2013). Falls have now replaced traffic accidents and physical assault as the leading cause of TBI in the community (Feigin *et al.*, 2013). Data from the US Centers for Disease Control and Prevention have shown that 51% of the cases of TBI in later life are due to falls, while the second most frequent cause, motor vehicle accidents, account for 9% of all cases (Thompson *et al.*, 2006). Death continues to be a common outcome of TBI (Stein *et al.*, 2010), with lethality being particularly high in older age groups. For example, the annual rate per 100,000 of TBI-related death caused by a fall increases from 1.0 in the age group 35-44 years to 6.8 in the age group 65-74 and 53.7 for those older than 85 years (Coronado *et al.*, 2011). Those who survive often have to negotiate the short and long term consequences of TBI, including neuropsychiatric symptoms. For example, among 1,438,339 people born in Denmark between 1977-2000 (N=1,438,339), 113,906 (7.9%) had a recorded hospital contact for TBI between 1977-2010 (Orlovskaja *et al.*, 2014). Those who had suffered a TBI showed higher incidence of organic mental disorders, as well as a surprisingly high incidence rate of schizophrenia, depressive and bipolar disorders. The increased risk ratio of schizophrenia and depressive disorders was associated with both mild and severe TBI (Orlovskaja *et al.*, 2014).

There is also evidence that exposure to TBI accelerates the cognitive decline associated with increasing age (Corkin *et al.*, 1989), and that this may increase the risk of dementia in general, and of Alzheimer's disease (AD) in particular (Plassman *et al.*, 2000). For example, current epidemiological evidence indicates that nearly 1 in every 3 people who die as a consequence of TBI have amyloid- β plaques in their brains (Sivanandam and Thakur, 2012), and that the deposition of

amyloid- β is detectable within hours of the injury (Johnson *et al.*, 2010). Amyloid- β plaques are one of the hallmarks of AD. TBI also seems to increase by 30% the risk of future stroke among survivors (Burke *et al.*, 2013), suggesting that cerebrovascular disease may offer an additional pathway linking TBI to cognitive decline and dementia. Masel and DeWitt suggested that TBI is better understood not as an event, but as a chronic disease process that triggers maladaptive neuroplastic changes (Masel and DeWitt, 2010). Such remodeling of the brain could conceivably undermine the person's cognitive reserve and erode resilience mechanisms, thus explaining the association between TBI and the late onset of neuropsychiatric disorders such as dementia and depression. However, it is uncertain whether the association between TBI and mental health outcomes would apply equally to a community-derived sample of older people, particularly when the injury occurs earlier in life. The issue, in this case, is that community-dwelling people who reach older age following a TBI might either have experienced a clinically insignificant event or might have been healthier than their peers who died early. Consequently, it is conceivable that the association between TBI and neuropsychiatric disorders could potentially weaken as the age of the population under investigation increases.

We used a community-derived sample of older men to determine: (1) the prevalence of TBI, (2) the association between history of past TBI and sociodemographic, lifestyle and clinical factors, (3) the risk of depression and cognitive impairment associated with exposure to TBI.

METHODS

Study design and setting

This investigation reports cross-sectional data on a community-derived sample of older men living in metropolitan Perth, Western Australia.

Participants

The study sample consisted of 5,486 men aged 70-89 years who provided information about history of past TBI during the second wave of assessments of the Health In Men Study (HIMS) between 2001-2004. Details about the study design and cohort have been described elsewhere (Norman *et al.*, 2009).

This study followed the principles of the Declaration of Helsinki and was approved by the Ethics Committees of the University of Western Australia and of the Department of Health of Western Australia. Participants provided written informed consent.

Outcomes

This survey investigated three outcomes of interest: TBI, past and current depression, and cognitive impairment (Figure 1). We used two complementary approaches to ascertain the presence of TBI. The first consisted of asking participants whether they had ‘ever suffered a blow to the head which caused you to become unconscious’ (yes/no). In addition, we used the Western Australian Data Linkage System (WADLS) to ascertain whether men had a recorded diagnosis of TBI during a previous contact with the health services (Holman *et al.*, 2008). The following International Classification of Diseases (ICD) codes identified relevant cases: 850 to 854 (ICD-9 codes for concussion, cerebral laceration and contusion, subarachnoid/subdural/extradural haemorrhage following injury, other or unspecified intracranial haemorrhage following injury, and intracranial injury or other unspecified nature) and S06 to S09 (ICD-10 codes for intracranial injury, crushing head injury, traumatic amputation of part of head, and other or unspecified injuries of head). WADLS data were available for the period between 1980 and the date of assessment for HIMS. We considered that participants had experienced a TBI if they had a recorded past medical contact in WADLS consistent with this diagnosis or if they answered ‘yes’ to direct questioning about having lost consciousness as a consequence of a blow to the head. Such a complementary approach to the

assessment of TBI is thought to yield more accurate information than the use of either approach in isolation (Feigin *et al.*, 2013).

We used three complementary strategies to identify men with current or past clinically significant symptoms of depression: (i) recorded diagnosis of a depressive episode in WADLS prior to assessment (ICD-9 codes 296.2, 296.3, 296.82, 296.90, 298.0 and 311, and ICD-10 codes F32, F33, F34.1 and F38.10), (ii) response in the affirmative to the question ‘*In the last 5 years, have you ever been told for the first time by a doctor that you have depression?*’, or (iii) a total score of 7 or greater on the 15-item version of the Geriatric Depression Scale (GDS-15) at assessment (Almeida and Almeida, 1999). We used this information to classify participants as never depressed, past depression (as per WADLS or self-reported past history), and current depression (GDS-15 ≥ 7). Past studies have shown that WADLS yields accurate diagnoses for severe mental disorders (Jablensky *et al.*, 2005). The mental composite score (MCS) was not used because of its correlation with the GDS ($r=-0.6$), to avoid multiple comparisons, and because it is not clear at which point the scale indicates that clinically significant mental health symptoms are present.

The presence of cognitive impairment was determined by a past diagnosis of dementia in WADLS (ICD-9 code 290 or ICD-10 codes F00, F01, F02 and F03), or by a total score of 23 or less on the Mini-Mental State Examination (MMSE) (Tombaugh and McIntyre, 1992). MMSE scores were available for 3905 men.

FIGURE 1

Exposures at study entry

Participants provided information about their age (in years), educational attainment (incomplete vs complete high school education), smoking (never, past or current), and alcohol use (no or

occasional use, 1-14 drinks/week, 15-27 drinks/week, 28 or more drinks/week). Data on alcohol use were collected during the 1996-1998 assessment, which occurred 5.7 years earlier (range 3.2 to 8.2 years). We considered that participants had hypertension if their systolic blood pressure was ≥ 140 or their diastolic blood pressure was ≥ 90 , or if they reported having been advised by their doctor that they had hypertension. The presence of diabetes was ascertained by asking participants if a doctor had ever told them that they had diabetes or if they reported treatment to lower blood sugar. Similarly, men indicated whether a doctor had ever told them that they had had a stroke, or a heart attack or angina (which we considered indicative of the presence of coronary heart disease).

Participants completed the SF-36 health survey, which we used to calculate the physical composite score (PCS) (Ware *et al.*, 1998). PCS scores range from 0 to 100, and the mean score for the general population is 50 (standard deviation = 10) (Ware *et al.*, 1998). Finally, we asked participants if they had had a '*fall to the ground in the last 12 months*' (yes/no) or if they had '*been injured as a result of a fall during the last 12 months*' (yes/no). An affirmative answer to either of these two questions was considered indicative of a fall during the preceding 12 months.

Statistical methods

We used the statistical package Stata/IC 13.1 to manage and analyse the data (StataCorp LP, 2013). Descriptive statistics summarised categorical data as count and proportions (%), and continuous variables as mean, range, and standard deviation of the mean (SD). We used the proportion command of Stata to estimate the prevalence of TBI, depression and cognitive impairment in the sample (95% confidence intervals – 95%CI – were calculated using a logit transformation that allows for the estimation of the standard error of the proportion), and logistic regression to calculate the odds ratio (OR) and 95%CI of the OR of the clinical outcomes according to the relevant exposures. Statistical adjustments for confounding variables were made using multiple logistic regression, and included factors associated with TBI, depression or cognitive impairment in

univariate analyses. Measured factors included age, education, smoking, alcohol use, hypertension, diabetes, coronary heart disease, stroke, falls and PCS scores. We calculated population fractions of depression and cognitive impairment attributable to TBI using the ‘punaf’ command (Newson, 2013). These analyses assume that the exposure (e.g., TBI) is causally related to the outcome (e.g., depression). Alpha was set at 5%.

RESULTS

The mean age of the 5486 participants was 77.3 years (SD=3.7), and ranged from 70 to 88 years. 953 men (17.4%, 95%CI=16.4%, 18.4%) were exposed to TBI. Of these, 790 reported TBI associated with loss of consciousness (14.6%, 95%CI=13.7%, 15.6%) and 230 (4.2%, 95%CI=3.7%, 4.8%) had a health service contact associated with TBI between 1980 and the study assessment. The prevalence of clinically significant depression (past or current) and of cognitive impairment was 14.5% (95%CI=13.6%, 15.4%) and 12.9% (95%CI=12.1%, 13.9%). Table 1 summarises the sociodemographic, lifestyle and clinical characteristics of participants.

TABLE 1

The prevalence of clinically significant depression (past or current) in men with and without a history of past TBI was 20.6% (95%CI=18.1%, 23.3%) and 13.2% (95%CI=12.2%, 14.2%). Self-reported history of TBI associated with loss of consciousness increased the odds of past and current depression even after statistical adjustments (Table 2). TBI associated with a health service contact increased the odds of past and current depression, but this association was not statistically significant once other measured factors were taken into account (Table 2). TBI of either form (self-reported or recorded in WADLS) was associated with increased odds of past and current depression after adjustment for confounding (Table 2). The population fractions of past and current depression attributable to TBI were for 5.0% (95%CI=1.7%, 9.5%) and 8.7% (95%CI=4.0%, 13.3%). Similarly,

the population fraction of prevalent depression (past or current) attributable to TBI was 6.9% (95%CI=3.3%, 10.3%).

The prevalence of cognitive impairment among men with and without a history of TBI was 15.6% (95%CI=13.5%, 18.1%) and 12.4% (95%CI= 11.4%, 13.4%). Self-reported TBI was not associated with increased odds of cognitive impairment, but WADLS recorded TBI was (Table 2). The strength of this association decreased when both definitions of TBI were considered, but remained statistically significant. The population fraction of cognitive impairment attributable to TBI was 3.4% (95%CI=0%, 6.9%) (Table 2).

TBI and cognitive impairment showed no evidence of interaction in modulating the risk of past (crude OR=1.22, 95%CI=0.66, 2.26) or current depression (crude OR=1.15, 95%CI=0.65, 2.03) and, similarly, history of past or current depression did not interact with TBI to modulate the risk of cognitive impairment (p=0.534 and p=0.630, respectively – same odds as that of the interaction between TBI and cognitive impairment).

Finally, we completed sensitivity analyses to clarify whether the association of TBI with depression and cognitive impairment changed after the exclusion of the 6 men who had experienced a TBI during the two years preceding the study assessment. The odds ratio of past and current depression associated with TBI were 1.82 (95%CI=1.19, 2.79) and 2.01 (95%CI=1.35, 3.16), whereas the adjusted odds ratio of cognitive impairment was 1.23 (95%CI=1.00, 1.51; adjusted for past stroke, falls and PCS score).

TABLE 2

DISCUSSION

The results of this study showed that 17% of men aged 70-88 years who are living in the community have experienced a clinically significant TBI. Depression (past or current) affected 14% of the sample and cognitive impairment 13%. More men exposed than not exposed to TBI showed evidence of depression and cognitive impairment (21% and 16% respectively), and among these cases 7% and 3% could be attributed to TBI.

Strengths and limitations

This study reports data on a large community-derived sample of older men for whom past and current clinical histories were available both from self-report and from health service contacts. In addition, we were able to include in our analyses other relevant measures, thus mitigating the potential confounding effect of concurrent clinical morbidities and lifestyle on the association between TBI and depression or cognitive impairment. The observed prevalence of TBI (17%) was relatively high, possibly because of the serial inclusion of self-report and hospital morbidity data. In contrast, the number of men with lifetime prevalent depression was somewhat low (14%), which may be due to the fact that only men were included, over-inflation of previously reported results, or low sensitivity of our ascertainment methods. If the latter is correct, then the power of our analyses to investigate the association between TBI and depression would have been compromised. Finally, the number of men with cognitive impairment was slightly high (13%), which may indicate that some false negative cases of cognitive impairment might have been included. If such misclassification has indeed occurred, then the odds of the association between TBI and cognitive impairment could be higher than observed. Although we cannot dismiss such a possibility, it is important to note that our results may simply reflect the fact that we have assessed 'cognitive impairment' rather than dementia in this sample. Furthermore, as far as we are aware, this is the largest survey ever designed to investigate the association between TBI and mental health outcomes of an unselected sample of older men.

The cross-sectional design of the study hinders our ability to infer causality from the associations observed, and the possibility of reverse causality cannot be dismissed. For example, depression and antidepressants have been associated with increased risk of falls (Kerse *et al.*, 2008), and it is conceivable that these could have preceded a TBI in at least some cases. The same line of reasoning would apply to older adults with cognitive impairment (Tinetti *et al.*, 1995). We have attempted to address this issue by completing a sensitivity analysis that excluded men with a recorded history of TBI during the two years that preceded the assessment. The results remained largely unchanged, although only 6 men were excluded from the analyses using this approach.

We also concede that healthy participant bias in this study is likely (Almeida *et al.*, 2014, Almeida *et al.*, 2008). The consequence of such a bias would be the loss of men with more disabling TBI and depression or cognitive impairment. This would lead to decreased prevalence of TBI, depression and cognitive impairment, as well as loss of power to investigate associations. Hence, our prevalence and risk estimates may be conservative. We also acknowledge that this study was limited to men. Current epidemiological evidence indicates that the psychiatric complications of TBI are largely independent of gender (Orlovska *et al.*, 2014), thereby suggesting that similar findings might be expected for women.

The link between depression (past or current) and TBI measured by self-report or data linkage was associated with similar effect sizes, although the association with current depression was more pronounced for self-reported than WADLS-recorded TBI. The converse was true for cognitive impairment. The effect of the association was more pronounced for TBI that led to a hospital contact, possibly because it was more severe. If that is indeed the case, these results would also suggest the presence of a dose-response effect (stronger association with more severe TBI that requires hospitalisation). It is worth noting that many people with hospital-recorded TBI do not self-

report, suggesting that surveys that rely solely on hospital morbidity data may underestimate the true prevalence of TBI in the community (Feigin *et al.*, 2013).

Finally, we acknowledge that our assessment of depression was not based on a structured clinical interview and does not necessarily equate to a diagnosis of depressive disorder according to DSM criteria. Nonetheless, our definition was consistent with what health professionals would consider ‘clinically significant’ and, in the case of current depression, our approach has been shown to have good face validity (Almeida and Almeida, 1999). The same applies to the study definition of cognitive impairment (Tombaugh and McIntyre, 1992).

Interpretation of the results

After considering the potential caveats associated with the design, procedures and measures of the study, we would suggest that our findings are consistent with the hypothesis that TBI increases the risk of clinically significant depression and cognitive impairment in older men. The risk of depression associated with TBI in our sample was similar in size to that described for younger adults in Denmark (Orlovska *et al.*, 2014) and for World War II American veterans (Holsinger *et al.*, 2002). This increase in risk, if causal, would account for about 7% of the cases of depression in later life (we acknowledge that the statistical methods used most likely inflate the true proportion of depression and cognitive impairment attributable to TBI). Similarly, a meta-analysis of 11 case-control studies investigating the association between TBI and dementia yielded a pooled unadjusted risk ratio of 1.82 (95%CI=1.26, 2.67) (Mortimer *et al.*, 1991), which is within the range of our analyses for TBI associated with a hospital contact. That meta-analysis also found that the association between TBI and dementia held for both early and late onset cases (age cut-point=70 years) and affected predominantly males (Fleminger *et al.*, 2003, Mortimer *et al.*, 1991). However, our data hints at the possibility that the association between TBI and cognitive impairment may not be as clear-cut if less severe forms of TBI are considered as exposures. This may explain why the

association between TBI and cognitive impairment (or dementia) seems less consistent than its association with depression (Moretti *et al.*, 2012).

The pathway linking TBI to depression is not clearly understood, but it is thought to involve pre-injury (such as psychosocial function, pre-existing mental disorders and lifestyle), injury (such as location and extension of brain lesions), and post-injury factors (such as post-concussive symptoms, neurological deficits – including cognitive impairment – and psychosocial function) (Silver *et al.*, 2009). TBIs associated with damage to the pre-frontal cortex and with multifocal white matter lesions have been associated with depression in some studies (Jorge *et al.*, 2004, Strain *et al.*, 2013), although others have suggested that depression is simply a non-specific brain response to stress and injury (Strakowski *et al.*, 2013). Loss of brain reserve as a result of TBI, rather than the location of lesions, has also been identified as a potential link between TBI and cognitive decline and dementia in later life (Moretti *et al.*, 2012). In this case, TBI would interact with other relevant risk factors to facilitate, rather than directly cause, dementia in older age (Moretti *et al.*, 2012).

Taken together, the findings of this study suggest that nearly 2 in every 10 men aged 70-88 years have been exposed to a clinically significant TBI, and that history of TBI is associated with greater risk of depression and cognitive impairment in later life. These findings are concerning, as the incidence of TBI seems to be rising (Coronado *et al.*, 2012) and this could potentially lead to an increase in the proportion of older people living with depression and cognitive impairment in the community. If we extrapolate our findings to the current Australian population (ABS, 2010), about 200,000 older people may have had or have depression as a consequence of TBI, whereas the number of cases of dementia among older Australians attributable to TBI would be of the order of 25,000 (for the USA, these figures should be multiplied by 13 (USDHHS, 2012)). Therefore, reducing the number of accidents leading to TBI could have important immediate and long-term implications for the health of the population (Chang *et al.*, 2004, Coronado *et al.*, 2012), and could

contribute to decrease the direct and indirect burden associated with depression and cognitive impairment in later life (Almeida *et al.*, 2013, Norton *et al.*, 2014). Future studies should aim to clarify if interventions that lead to a decrease in the prevalence of TBI (e.g., falls prevention programs) are also successful at reducing the prevalence of depression and cognitive impairment in later life.

Original publication

The authors declare this report contains original unpublished work that is not being considered for publication elsewhere.

Declaration of interests

The authors declare they have no conflicts of interest.

Roles and responsibilities

OPA conceived and designed the study. OPA, GJH, BBY, JG and LF performed the experiments. OPA analysed the data and drafted the manuscript. OPA, GJH, BBY, JG and LF reviewed the manuscript critically and approved its submission to the Journal.

Ethics approval

The Human Research Ethics Committees of the Royal Perth Hospital and of the Department of Health of Western Australia approved the research protocol and procedures of the study, which follow the principles of the Declaration of Helsinki. All participants provided written informed consent.

Access to data

Consent procedures and ethics approval restrict access to the data to named investigators.

Provenance and peer review

This is an investigator-initiated trial; not commissioned.

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Table 1. Sociodemographic, lifestyle and clinical characteristics of older men with past history of traumatic brain injury, and past or current history of depression or cognitive impairment.

	Population N=5486 n (%)	TBI N=953 n (%)	TBI OR (95% CI)	Depression N=793 n (%)	Depression OR (95% CI)	Cognitive Imp. n=710 n (%)	Cognitive Imp. OR (95% CI)
Age in years							
70-74	1911 (34.8)	330 (34.6)	1	227 (28.6)	1	193 (27.2)	1
75-79	2359 (43.0)	406 (42.6)	1.00 (0.85,1.17)	347 (43.8)	1.28 (1.07,1.53)	313 (44.1)	1.36 (1.13,1.65)
80+	1216 (22.2)	217 (22.8)	1.04 (0.86,1.26)	219 (27.6)	1.63 (1.33,1.99)	204 (28.7)	1.79 (1.45,2.22)
High school education	2521 (46.0)	446 (46.8)	1.04 (0.91,1.20)	338 (42.7)	0.86 (0.73,1.00)	237 (33.4)	0.55 (0.46,0.65)
Smoking							
never	1775 (32.4)	317 (33.3)	1	205 (22.8)	1	218 (30.7)	1
past	3420 (62.3)	588 (61.7)	0.95 (0.82,1.11)	528 (66.6)	1.40 (1.18,1.66)	456 (64.2)	1.10 (0.92,1.31)
current	291 (5.3)	48 (5.0)	0.91 (0.65,1.27)	60 (7.6)	1.99 (1.45,2.74)	36 (5.1)	1.01 (0.69,1.47)
Alcohol							
no/occasional	1585 (30.2)	294 (31.9)	1	279 (36.6)	1	250 (36.7)	1
1-14 drinks/week	2707 (51.6)	439 (47.7)	0.85 (0.72,1.00)	339 (44.4)	0.67 (0.56,0.80)	327 (47.9)	0.73 (0.61,0.88)
15-27 drinks/week	561 (10.7)	107 (11.6)	1.03 (0.81,1.32)	81 (10.6)	0.79 (0.60,1.03)	61 (8.9)	0.65 (0.48,0.88)
28+ drinks/week	394 (7.5)	81 (8.8)	1.14 (0.86,1.50)	64 (8.4)	0.91 (0.67,1.22)	44 (6.4)	0.67 (0.48,0.94)
Hypertension	1671 (30.5)	293 (30.7)	1.02 (0.87,1.18)	279 (35.2)	1.29 (1.10,1.51)	236 (33.2)	1.16 (0.98,1.37)
Diabetes	617 (11.3)	93 (9.8)	0.83 (0.66,1.04)	129 (16.3)	1.67 (1.36,2.07)	85 (12.0)	1.08 (0.85,1.38)
Coronary heart disease	1559 (28.5)	301 (31.7)	1.20 (1.03,1.40)	292 (37.0)	1.58 (1.35,1.85)	221 (31.2)	1.16 (0.98,1.38)
Stroke	410 (7.5)	97 (10.2)	1.53 (1.20,1.94)	112 (14.1)	2.43 (1.92,3.06)	79 (11.1)	1.68 (1.30,2.18)
Falls	1166 (21.4)	288 (30.5)	1.82 (1.55,2.13)	291 (37.0)	2.54 (2.16,2.99)	191 (27.1)	1.44 (1.20,1.73)
PCS < 50	4013 (76.8)	740 (80.7)	1.32 (1.11,1.58)	628 (87.1)	2.23 (1.78,2.80)	533 (80.6)	1.30 (1.06,1.59)

TBI: traumatic brain injury; Cognitive Imp.: cognitive impairment; PCS: physical composite summary of the SF-36; OR: odds ratio; 95% CI: 95% confidence interval of the odds ratio.

Bold print highlights statistically significant odds ratio.

Table 2. Risk of past and current depression, as well as cognitive impairment, associated with past history of traumatic brain injury (TBI).

	Population N=5486 n (%)	Past Depression N=404 n (%)	Current Depression N=359 n (%)	Cognitive Impairment N=710 n (%)
TBI (self-reported data only)	790 (14.6)	83 (20.8)	80 (23.0)	112 (16.1)
TBI crude odds ratio (95%CI)	1	1.69 (1.31,2.19)	1.93 (1.48,2.51)	1.14 (0.92,1.42)
TBI adjusted odds ratio 1 (95%CI)	1	1.53 (1.17,1.99)	1.82 (1.37,2.41)	1.09 (0.87,1.37)
TBI adjusted odds ratio 2 (95%CI)	1	1.53 (1.17,2.02)	1.90 (1.42,2.54)	1.14 (0.91,1.44)
TBI (hospital data only)	230 (4.2)	27 (6.7)	26 (7.2)	48 (6.8)
TBI crude odds ratio (95%CI)	1	1.84 (1.21,2.79)	2.01 (1.31,3.07)	1.83 (1.32,1.54)
TBI adjusted odds ratio 1 (95%CI)	1	1.60 (1.03,2.48)	1.51 (0.93,2.47)	1.69 (1.19,1.39)
TBI adjusted odds ratio 2 (95%CI)	1	1.56 (0.99,2.45)	1.50 (0.90,2.50)	1.68 (1.18,2.40)
TBI (self-reported or hospital data)	953 (17.4)	101 (25.0)	99 (27.6)	149 (21.0)
TBI crude odds ratio (95%CI)	1	1.76 (1.38,2.23)	2.01 (1.57,2.56)	1.31 (1.08,1.60)
TBI adjusted odds ratio 1 (95%CI)	1	1.55 (1.21,1.99)*	1.77 (1.36,2.32)‡	1.23 (1.00,1.51)†
TBI adjusted odds ratio 2 (95%CI)	1	1.56 (1.21,2.01)	1.82 (1.38,2.39)	1.27 (1.03,1.57)

95%CI: 95% confidence interval of the odds ratio.

Adjusted odds ratio 1: model adjusted for the presence of coronary heart disease (not included for cognitive impairment), stroke, falls and PCS < 50.

Adjusted odds ratio 2: model adjusted for all variables listed on table 1.

Adjusted odds ratio 1 of depression with additional adjustment for cognitive impairment: depression OR=1.53, 95%CI=1.20,1.97; depression OR=1.73, 95%CI=1.32,2.26.

Adjusted odds ratio 1 of depression with additional adjustment for cognitive impairment and sleep complaints: past OR=1.48, 95%CI=1.15,1.97; depression OR=1.56, 95%CI=1.18,2.06.

*Population fraction of past depression attributable to TBI = 5.0% (95%CI=1.7%,9.5%).

‡Population fraction of current depression attributable to TBI = 8.7% (95%CI=4.0%,13.3%).

†Population fraction of cognitive impairment attributable to TBI = 3.4% (95%CI=0.0%,6.9%).

Figure 1. The figure shows the source of endpoints for the study. Traumatic brain injury (TBI) data were obtained through direct questioning of participants during the 2001-2004 survey, as well as from health administrative data (WADLS) dating back to 1980. Similarly, during the 2001-2004 survey participants reported data on past clinically significant depressive symptoms and use of antidepressants, and completed the 15-item of Geriatric Depression Scale (GDS-15). WADLS provided additional data on past health contacts associated with a recorded diagnosis of a depressive disorder. Finally, during the 2001-2004 assessment, men completed the Mini-Mental State Examination (MMSE) – those with scores lower than 24 or with a recorded diagnosis of dementia in WADLS were considered to show evidence of cognitive impairment.