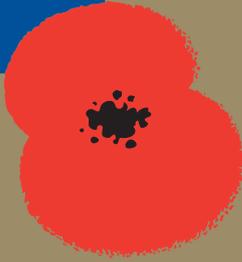


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# A case-control study examining the association between service-related mental ill-health and dementia in male military veterans over the age of 65





## Contents

Glossary of terms .....	2
Statistical terms .....	3
The King's Centre for Military Health Research (KCMHR).....	4
Acknowledgements.....	4
Executive Summary.....	6
Introduction.....	8
♦ Dementia .....	8
♦ Risk and protective factors associated with dementia .....	8
♦ Military risk and protective factors for dementia.....	10
♦ Objective .....	11
Design.....	13
♦ Ethical approval .....	13
♦ Recruitment.....	13
♦ Participant Selection.....	13
♦ Data Collection.....	15
♦ Data Analysis.....	17
Results .....	18
♦ Participants.....	18
♦ Demographic factors.....	18
♦ Military factors .....	19
♦ Lifestyle factors.....	20
♦ Medical conditions .....	21
♦ Mental health conditions .....	22
Discussion.....	24
♦ Summary of results .....	24
♦ Healthy soldier effect.....	25
♦ Comparison with existing military literature .....	26
♦ Strengths.....	26
♦ Limitations .....	26
♦ Future research .....	26
Conclusion.....	27
References .....	28

## Glossary of terms

**KCMHR:** King's Centre for Military Health Research

**MoD:** Ministry of Defence

**RBL:** Royal British Legion

**MDD:** Major Depressive Disorder

**PTSD:** Post Traumatic Stress Disorder

**BMI:** Body Mass Index

**NICE:** National Institute for Health and Care Excellence

**TBI:** Traumatic Brain Injury

**mTBI:** mild Traumatic Brain Injury

**LSC:** Long-Standing Companion

**CHRN:** Care Home Research Network

**MMSE:** Mini-Mental State Examination

**GP:** General Practitioner

**RAF:** Royal Air Force

**MH:** Mental Health

**CMD:** Common Mental Disorders

## Statistical terms

Statistical acronym	Explanation
<b>Statistically significant difference</b>	The difference between two groups is statistically significant if the p value is equal to, or less than, 0.05 (i.e. there is a less than 5% chance that the two groups are not different). This means that the difference between the groups cannot be explained by chance alone but must be caused by something else.
<b>Standard deviation</b>	This value is used to explain how much the individual values within a group differ from the mean value.
<b>Interquartile range</b>	This value is similar to the standard deviation but is used in collaboration with a median. It is used to explain how much individual values within a group differ from the median value.
<b><math>\chi^2</math> (chi squared) test</b>	A test to show a relationship between categorical (two distinctly different) variables. The result tells you whether the difference between categorical variables is more or less than you would expect to see if there were no relationship (simply by chance).
<b>Fischer's exact test</b>	A test to show a relationship between categorical variables for small sample sizes. The result tells you whether the difference between categorical variables is more or less than you would expect to see if there were no relationship (simply by chance).
<b>Wilcoxon Mann Whitney U Test</b>	A test to show a relationship between the median values of a continuous variable. The result tells you whether the difference between the median values is more or less than you would expect to see if there were no relationship (simply by chance).
<b>T test</b>	A test to show a relationship between two mean values of a continuous variable. The result tells you whether the difference between the mean values is more or less than you would expect to see if there were no relationship (simply by chance).

## King's Centre for Military Health Research (KCMHR)

Previously the Gulf War Illness Research Unit, the King's Centre for Military Health Research (KCMHR) was launched in 2004 as a joint initiative between the Institute of Psychiatry and the Department of War Studies, King's College London. KCMHR draws upon the experience of a multi-disciplinary team and is led by Professor Sir Simon Wessely and Professor Nicola T. Fear. The centre undertakes a wide range of research investigating military life using quantitative and qualitative methods. Its flagship study is an ongoing epidemiological multiphase investigation of the health and wellbeing of approximately 20,000 UK Armed Forces personnel. The study, funded by the Ministry of Defence (MoD), has been running since 2003 and the results from the third phase of data collection have recently been published. Data from our studies have been used to analyse various military issues, and many

hundreds of academic papers have been published in peer reviewed, scientific journals. Our findings are regularly reported in the press and have also been used to inform military, health service and charitable policy makers. KCMHR also maintains excellent links with other academic centres across the globe.

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## Acknowledgements

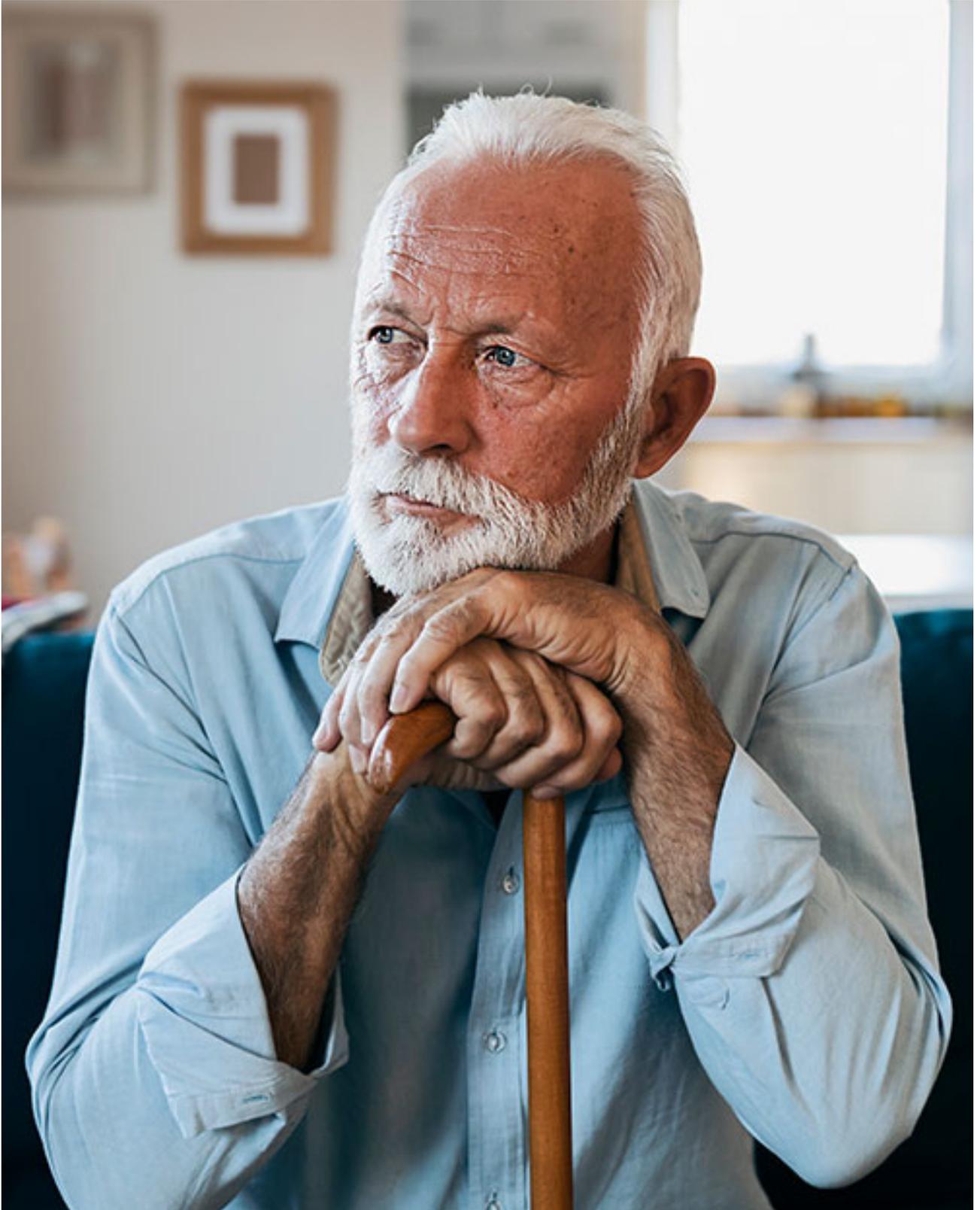
This research would have not been possible without the generous involvement of the people who participated in this study. Their honesty and openness allowed the frank conversations upon which this research is built.

It is important to highlight that the quotes and opinions of the participants included in this research do not necessarily reflect those of the research team, or KCMHR more generally.

In addition to the listed authors the study involved support from the wider team at KCMHR including, but not limited to Prof. Nicola T. Fear, Prof. Sir Simon Wessely, David Pernet, Richard Turner, Alison McKinlay, Christopher Albertyn,

Hannah Harwood, Bethany Croak, Demos Christou, Tatyana Abraham, Philip Sharma, Christopher Jones, Heather Staples, Hannah Neitzel, Rebecca Akhanemhe, Ryan Leone, Chelsea Honeyman and Lewis McCaffrey.

We are grateful to the Ministry of Defence, Armed Covenant and the Royal British Legion (RBL) Aged Veterans Fund for funding the research and for their excellent support and engagement throughout the project, especially from Paula Smith the RBL Senior Admiral Nurse. We would also like to pay particular thanks to James Grassom from the Join Dementia Research database for his continued support with the recruitment for the study.



# Executive Summary

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## Introduction

Dementia is currently incurable, irreversible and a major cause of disability for the world's older population. The identification, and early intervention of modifiable risk factors, is therefore of increasing global priority. Prior scientific studies have suggested numerous risk factors which increase the chance of developing dementia, a number of which are suggested to occur at a greater frequency within military and military veteran personnel. One such risk factor is service-related mental ill health.

This project aimed to determine whether service-related mental ill-health increases the risk that male military veterans have of developing dementia. The study compared the prevalence of service-related mental ill-health in male military veterans with dementia with those without dementia.

## Design

The project employed a mixed methods case control design.

- Case group: male veterans with dementia: must have served a minimum of 2 years as a regular in the UK Armed Forces, be aged 65 or over, have a formal diagnosis of dementia
- Control group: male veterans without dementia: must have served a minimum of 2 years as a regular in the UK Armed Forces, be aged 65 or over and have no formal diagnosis of dementia

Participants were recruited to the study through a variety of strategies: via care homes; through Join Dementia Research (a system which connects those with dementia, and their carers, with researchers); and through various community organisations attended by veterans (including Armed Forces breakfast clubs and coffee mornings).

Dementia diagnosis for case participants was ascertained from medical records. In addition to the absence of a dementia diagnosis, potential control group participants were asked to complete the Mini-Mental State Examination (MMSE) to further ensure that they did not have poor cognitive function which might indicate a potential dementia diagnosis.

Qualitative interviews were held with both groups of veterans to explore their experience of mental ill health both during and after service. Interviews were also conducted with long standing companions, of each veteran, who were individuals who knew the veteran well (for example, spouse, child or close friend) and were in regular contact with the veteran (at least one contact in the last month). These interviews were supplemented with data drawn from military service and medical records and civilian medical records to identify service-related mental ill health as well as a range of factors including:

- Demographic factors: age; relationship status; number of children
- Lifestyle factors: physical activity; obesity; social activity; educational attainment; cognitive complexity of occupations; smoking; alcohol consumption
- Medical conditions: mild traumatic brain injury (mTBI); cardiovascular conditions and risk factors; hearing impairment
- Military factors: service branch; rank; length of service; number of deployments; combat exposure

## Results and Discussion

121 male military veterans were included in the final analysis reported: 48 cases (diagnosis of dementia) and 73 controls (no diagnosis of dementia). The mean age of participants in the

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dementia group (case) was 82 and 80 in the non-dementia (control) group; the oldest veteran was 100 years old.

There were no differences between the dementia and non-dementia group related to experiencing mental ill health which included both self-reported mental health difficulties and diagnosed mental health conditions. Service-related mental-ill health was not seen at a higher level in those with dementia when compared to those without dementia.

However, participants in the non-dementia group were more likely to be single and to be overweight, both of which are risk factors for dementia.

At first glance, it may appear counter-intuitive for known dementia risk factors to occur more commonly in the group without dementia, however exploration of the military factors investigated may help to explain these findings. First, those in the dementia group were more likely to have served in the Armed Forces only as part of national service (conscripted to join the Armed Forces and served less than 3 years). Second, those with dementia were more likely to have served in the Armed Forces for less time (11 years in the dementia group versus 16 years in the non-dementia group) and third they were less likely to report having experienced combat exposure (whether participants ever seriously thought that they might be killed or witnessed someone being killed or seriously injured). From this it could be concluded that the dementia group had a 'military-light' experience when compared to those in the non-dementia group.

One potential explanation for not seeing higher levels of putative dementia risk factors in the dementia group, alongside seeing higher levels in the non-dementia group for obesity and single

relationship status, may be the healthy soldier effect. The healthy soldier effect relates to the high level of physical fitness required for entry into the Armed Forces, the requirement to maintain high levels of physical activity during service and frequent medical examinations during service, which impact the mortality and morbidity of the Armed Forces in comparison to the general population. It is estimated that the healthy soldier effect equates to a reduction in mortality of between 10 and 25% when compared to the general population. The healthy soldier effect may also mask, partially or completely, any increased risk of dementia within the military veteran population. Whilst the healthy soldier effect holds true for career soldiers, those who served in the Armed Forces as part of national service would not have been subject to the same degree of physical fitness, activity or health screening. As the dementia group contains a higher proportion of national service soldiers, it may be that the healthy soldier effect is less apparent within this group.

## **Conclusion**

This study found no evidence for an association between mental ill health in service and dementia. Our finding may be attributed to the healthy soldier effect which may mask, or mitigate, any heightened risk factors for dementia within those who serve in the Armed Forces. Further research examining older veterans, but excluding those who only served as part of national service, in comparison to the general population is needed to further examine the role of mental health conditions, as well as other risk factors, with dementia within the military veteran population in the UK.

# Introduction

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## **Dementia**

Dementia is currently incurable, irreversible and a major cause of disability for the world's older population. Dementia is caused by degeneration of the brain and is characterised by symptoms such as memory loss, language difficulties and reduced problem-solving ability (Alzheimer's Society, 2014). Dementia is currently irreversible and progressive meaning that symptoms continue to worsen throughout the patient's life (Alzheimer's Society, 2014). According to the Alzheimer's Society (2014) the number of people affected by dementia in the UK general population is estimated to be about 850,000, affecting 1 in every 14 people over the age of 65. Age is the biggest risk factor for dementia with the risk doubling every 5 years after the age of 65 (Alzheimer's Society, 2014). Dementia prevalence is increasing; the number of people living with dementia in the UK is estimated to reach over 1 million by 2025, and over 2 million by 2050 (Lewis et al. 2014). This rise comes at both a personal cost to people with dementia, and their families and carers, but also a huge economic cost to the UK. The current financial cost of dementia to the UK economy is over £24 billion a year resulting from a combination of health and care costs and the vast contribution made by informal carers (Lewis et al. 2014). We also know that people with dementia have a lower self-reported quality of life than both the general population as a whole and when compared to those over 65 without dementia (Lewis et al. 2014).

## **Risk and protective factors associated with dementia**

The identification and early intervention of modifiable risk factors for dementia are of increasing priority worldwide and recent academic work has centred on highlighting and understanding such risk factors (Livingston et al., 2017).

## ***Mental Health Conditions***

Major Depressive Disorder (MDD) has been emphasised as a risk factor for dementia in a number of systematic reviews (Bellou et al., 2017; Baumgart et al., 2015; Barnes et al., 2011), suggesting that within the civilian population those with a diagnosis of MDD are twice as likely to develop dementia (Ownby et al., 2006).

Whilst Post traumatic stress disorder (PTSD) has not been highlighted as a dominant risk factor within general population reviews, empirical evidence is amassing which stresses the importance of the association between PTSD and dementia across a range of populations. A study of 9/11 survivors found that current PTSD, as well as MDD diagnosis, was associated with a two-fold increase in cognitive impairment (Clouston et al., 2016). Holocaust survivors with PTSD have been shown to demonstrate accelerated aging compared to both holocaust survivors without PTSD and 'healthy' controls (Golier et al., 2002).

In addition to the experience of mental disorders, the treatment of mental disorders, particularly through the use of benzodiazepines (typically prescribed to treat sleep disorders and anxiety disorders) and psychotropic medications (typically prescribed to treat depression, anxiety and psychosis), has been suggested to increase the risk of developing dementia (Bellou et al., 2017; Billioti de Gage et al., 2012; He et al., 2019; Mawanda et al., 2017).

## ***Lifestyle factors***

Living a healthy lifestyle has been shown to act in a protective fashion against the development of dementia, whilst engaging in less healthy habits appears to increase the risk of developing dementia. Activities which are both physically and mentally engaging, such as taking part in multiple leisure activities every week (Podewils et al., 2005; Rovio



et al., 2005) and working in a complex occupational role (Andel et al., 2005) have been shown to reduce the risk, or protect against, the development of dementia.

Those individuals who engage in less physically and mentally engaging activities, such as those who are obese in mid-life (Loef and Walach, 2012), have a low level of educational attainment (Schoenhofen-Sharp and Gatz, 2011) and those have a low level of social participation and social contact (Kuiper et al., 2015; Bellou et al., 2017) as well as those who engage in unhealthy habits such as smoking (Barnes and Yaffe, 2011) and heavy or 'binge' drinking (Yaffe et al., 2014; NICE, 2015), appear to be at an increased risk of developing dementia.

### ***Medical conditions***

Hearing loss has been associated with an increased risk of dementia across numerous studies (Thomson et al., 2017; Lin and Martin, 2014). Cardiovascular conditions such as heart disease and strokes (Justin et al., 2013), and cardiovascular risk factors including hypertension (Sharp et al., 2011) and diabetes (Biessels et al., 2006) (as well as smoking and obesity outlined above) are all associated with an increased risk of dementia. Mild traumatic brain injury (mTBI), which is defined as a knock to head accompanied by being dazed, an inability to remember the injury, or a loss of consciousness has been shown to increase the risk of dementia (Wang et al., 2012) although the evidence is as yet not universally supportive of this association (Dams-O'Connor et al., 2013).

### **Military risk and protective factors for dementia**

A recent review of the literature by the King's Centre for Military Health Research (Rafferty et al., 2018) highlighted a series of risk and protective factors for dementia which are found at an increased level in the military veteran population when compared to the general population.

### ***Mental health conditions***

Notably, Common Mental Disorders (CMD), including anxiety and depression, are reported to occur at an increased rate in military personnel compared to the general population. Indeed, within the UK Goodwin et al (2015) found that the risk of CMD is approximately twice within the military population as compared to the general population in employment, although these comparisons do not take account of the often challenging backgrounds of those joining the Armed Forces. Rates of PTSD within UK military personnel are approximately 6%, which is slightly higher than seen in the general population (~4%) (Stevellink et al., 2018). Therefore if, as civilian literature suggests, mental disorders such as depression and PTSD do represent risk factors for dementia, then military personnel may represent a population with an increased vulnerability.

Studies of US military veterans indicate that veterans with a diagnosis of either PTSD or MDD are at a significantly greater risk of developing dementia than 'healthy' controls (Byers et al., 2012; Yaffe et al., 2010; Qureshi et al., 2010).

### ***Lifestyle factors***

Serving military personnel may be thought of as engaging in a healthy lifestyle characterised by both physically diverse activities and a high degree of comradery and companionship. Yet, military service is not unilaterally synonymous with a healthy lifestyle. The use of alcohol within the Armed Forces population has long been a contentious issue. Research exploring the trajectories of alcohol users in the Armed Forces found that heavy drinkers failed to reduce their drinking pattern over a period of eight years, suggesting that such behaviours are engrained and would be unlikely to change upon transition out of the Armed Forces (Goodwin et al., 2017). Indeed, veterans report higher levels of hazardous drinking, with a greater risk of alcohol dependence and alcohol related harm than Armed Forces personnel, and a greater degree of alcohol

misuse than seen in the general population (Murphy and Turgoose, 2018).

Information from the Annual Population Survey of UK Armed Forces Veterans residing in Great Britain, 2017 (Ministry of Defence, 2019) shows that veterans of retirement age were more likely to have ever smoked than non-veterans of retirement age (66% vs 56% respectively), and the same was true for veterans of working age when compared to non-veterans of working age (55% vs 44% respectively).

Upon transition out of the Armed Forces, and out of a structured lifestyle, some veterans fail to keep up the same levels of physical activity. Indeed, within the US veteran population an epidemic of retirement obesity has been reported (Yaffe et al., 2014). For some their time in military service may have resulted in physical impairments such as chronic arthritis and other musculoskeletal complaints, which may impact their ability to engage in physical activity post-service (Williamson et al., 2019).

Those who join the Armed Forces are less likely to hold a degree when compared to the general population (21% compared to 30% respectively) (Ministry of Defence, 2019). And upon leaving the military veterans are more likely to hold 'blue collar' roles such as working in 'process, plant and machine operation' compared to the general population (18% and 8% respectively), and are less likely to work in more complex 'white collar' or 'professional occupations than the general population (11% compared to 20%) (Ministry of Defence, 2019). Many UK veterans also report that leaving the Armed Forces and trying to integrate into a civilian world can result in feelings of loneliness or social isolation (TRBL, 2014; TRBL, 2018; SSAFA, 2017; Wilson and Kiernan, 2018).

### **Medical conditions**

Exposures during military service may result in an increased rate of certain medical conditions including both hearing loss (Royal British Legion,

2014) and mTBI, than seen in the general population (Veitch et al. 2013; Weiner et al. 2013; Byers & Yaffe, 2014; Sibener et al. 2014).

In particular, those veterans experiencing a mental disorder appear to have a higher prevalence of hearing loss (Parker et al., 2020) and mTBI (Rona et al., 2012) than the veteran population as a whole, as well as other conditions such as metabolic syndrome (Sharp et al., 2019; Dyball et al., 2019; Williamson et al., 2019) and higher rates of smoking (Dyball et al., 2019).

Despite the potential relationship between mental conditions and dementia demonstrated within the civilian and US military veteran populations, and the increased exposure to a range of other dementia risk factors for military veterans, to date there has been no research exploring the relationship between mental ill health and dementia within UK military veterans.

### **Objective**

The current study aimed to explore the relationship between mental ill-health during military service and dementia within the UK military veteran population.

- To ascertain whether service-related mental ill-health places military veterans at an increased risk of developing dementia via comparison of service-related mental ill-health in military veterans over the age of 65 with dementia and a control group of military veterans over the age of 65 without dementia.
- To identify whether other risk factors, which may occur at a heightened degree within a military veteran population, have an impact on the relationship between service-related mental ill-health and later onset of dementia.



# Design

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## **Design**

This project employed a mixed-methods approach, utilising both a qualitative exploration of elderly veterans' mental well-being, corroborated with a Long-Standing Companion (LSC) interview, and quantitative evidence drawn from veterans' medical and military service records.

## **Ethical approval**

Ethical approval was granted by the Psychiatry, Psychology and Neuroscience Research Ethics Subcommittee at King's College London (Reference: RESCM-17/18-5184) as well as from the Health Research Authority Social Care Research Ethics Committee (Reference: 18/IEC08/0044).

## **Recruitment**

Participants were recruited to the study through a variety of strategies: via care homes; through Join Dementia Research; and through various community organisations as described below.

### ***Care homes***

Multiple UK-based care homes were approached using existing links with the Royal British Legion, Royal Star & Garter, Royal British Legion Industries and the Care Home Research Network (CHRN). Members of the research team visited each care home and delivered a presentation outlining the research project and the eligibility criteria for participants, handing out pamphlets with more detailed information. Residents of care homes logged their interest with members of care home staff which were then sent onto the research team.

### ***Join Dementia Research***

Advertisements were placed on Join Dementia Research, a system which connects those with dementia and their carers, with researchers. Advertisements provided information on the research project and the eligibility criteria for participants. Those who were interested in taking part logged their interest on the Join Dementia Research system and the research team received their contact information.

### ***Community organisations***

Social organisations setup for military veterans and/ or those with dementia were contacted and provided with information about the research project and the eligibility criteria for participants. Members of the research team then visited the organisations when military veterans and/ or those with dementia might be attending, for example coffee mornings, to provide a brief presentation on the research project. If this was not possible then information was sent to the organisations to pass onto potential participants with the contact information of the research team. Those who were interested in taking part in the research got in touch with the research team either face to face after the briefing presentation, or via the contact details they had been provided with.

## **Participant Selection**

Participants were deemed eligible to take part in the study if they met the following criteria for either the case group or the control group.

### ***Eligibility criteria***

#### **Case Group: Veterans with dementia**

- Age 65 or over
- Male
- Served as a regular in the military for a minimum of two years
- Had a formal diagnosis of dementia (according to McKhann et al. (1984) criteria) derived from their medical records
- Able to provide informed consent (either themselves, or via a consultee if they lacked capacity)
- Had an eligible LSC that could be contacted
- Fluent in English

#### **Control Group: Veterans without dementia**

- Age 65 or over
- Male
- Served as a regular in the military for a minimum of two years
- Did not have a formal diagnosis of dementia (according to McKhann et al. (1984) criteria)
- Able to provide informed consent
- Had an eligible LSC that could be contacted
- Fluent in English

For each participant the eligible LSC had to meet the following criteria:

#### **Long-standing companions**

- Age 18 or over
- Knew the veteran well (for example, spouse, child, close friend)
- In regular contact with the veteran; defined as at least one method of contact made in the last month (phone or physical visit)
- Able to provide informed consent
- Fluent in English

### ***Consent***

Consenting was an iterative process. Firstly, mental capacity was assessed, if a participant was deemed to have mental capacity to consent, the researcher sought written informed consent directly from the participant. If the participant was deemed to lack mental capacity to consent, a personal consultee was identified and approached (typically a family member or designated next of kin). An information sheet, declaration form and return envelope was sent to the elected personal consultee. Researchers gave them a courtesy follow-up call within five days to confirm receipt of the documents. Once contacted by telephone, the researcher asked about their decision to act as personal consultee and answered any questions.

If there had been a situation in which healthcare staff and/or the research team had concerns that a participant had lost their capacity to consent to being in the trial, the study team would have withdrawn the participant from the study; however no instances of this took place during the study.

Participants were able to withdraw from the study by phoning, emailing or writing to the research team.

### ***Dementia diagnosis***

Within the UK dementia is diagnosed by a medical professional based on symptoms including: impact on daily functioning (ability to judge, think, plan and organise); change in behaviour (emotional lability, irritability, apathy or deteriorating social skills); and demonstrating a decline over the course of several months or years (NHS England, 2015). If these symptoms are demonstrated a GP may conduct a brief screen using cognition tools (such as the Mini-Cog, the General Practitioner assessment of Cognition, the 6-CIT or the Montreal Cognitive Assessment

tool) and use these results in combination with a detailed history, examination and blood screening to enable a diagnosis, or referral on to specialised dementia services (NHS England, 2015).

Therefore, participants were assigned to the case group if they had a formal diagnosis of dementia on their medical records.

### ***Assessment of cognitive function***

Once written informed consent was obtained from the veteran, those veterans without a diagnosis of dementia were asked to complete the Mini-Mental State Examination (MMSE) to further ensure that those allocated as controls (without dementia) did not have poor cognitive function. A cut-off score of 24 or more on the MMSE indicates normal cognition. To be classified as a control for this study an MMSE score of 26 was required; borderline scores of 24 or 25 were discussed with a consultant older age psychiatrist (Dr Karla Greenberg). Such borderline scores may be indicative of poor cognition but could also be due to a physical limitation (i.e. poor motor skills, illiteracy). If a participant scored 23 or lower, research staff asked for the participant's consent to share this with care home staff as they may benefit from further medical investigation from their GP regarding their cognitive function. If their GP diagnosed dementia, then these individuals were given the opportunity to act as case participants. Those participants who scored 26 or above were included as control participants.

## **Data Collection**

### ***Military and medical records***

Participants with mental capacity were asked to complete forms to request their military service records and their medical records from their GP. For those without capacity these forms were

completed by the personal consultee. Once received key variables of interest were extracted from the medical and service records as outlined below:

- Mental health: diagnosis of MDD and/ or PTSD; mental health medication history (benzodiazepine prescriptions, extended use of psychotropic medication)
- Medical conditions: mild traumatic brain injury (mTBI); cardiovascular conditions and risk factors; hearing impairment
- Military factors: military branch; primary role; rank upon leaving; length of service; deployment history

### ***Veteran Interviews***

Interviews with veterans took place face to face at a time and location convenient for the veteran. Interviews typically lasted around an hour. Interviews focused on exploring the nature of the veteran's mental well-being and targeting potential symptoms of mental ill-health, both during service and after leaving the Armed Forces. Any mental health difficulties such as low mood or traumatic experiences were explored further to ascertain whether they might represent potential undiagnosed PTSD or MDD. Potential undiagnosed PTSD was defined as experiencing a traumatic event in combination with the report of symptoms of PTSD such as: change to day to day life; affect on motivation; affect on sleep; flashbacks; affect emotionally; affect on exercise; affect on appetite; thinking about trauma when not wanting to; becoming anxious/ upset; avoiding the subject/ location. Potential undiagnosed MDD was defined as an experience of low mood in combination with the report of symptoms of MDD such as: persistent low mood; change to day to day life; affect on motivation; thoughts of harming self; suicidal thoughts.



Additional information on demographic factors, lifestyle factors, medical conditions and military factors of interest were also collected as summarised below:

- Demographic: age; relationship status; number of children
- Lifestyle: physical activity; weight; social activity; education; occupation post-service; smoking status; alcohol consumption; substance abuse
- Medical conditions: mTBI (a knock to the head plus either: dazed; failing to remember incident; or loss of consciousness); hearing impairment
- Military factors: combat exposure (whether participants ever seriously thought that they might be killed or witnessed someone being killed or seriously injured)

### ***Interviews with Long Standing Companions (LSCs)***

The LSC of each veteran participant was asked to complete the Cornell Scale for Depression. The Cornell Scale is a measure of depression that a significant other completes in reference to the mood state of another individual. In this study the LSC completed the scale in relation to the military veterans' mood state. A probable case of current MDD is defined as a score of between 10 and 18, with a score of below 10 defined as not a case (Alexopoulos, 2002).

LSCs also participated in an interview, typically over the phone, at a time convenient to them. These interviews lasted between 30 and 45mins. The LSC interviews asked the same questions as the veteran interview to create a secondary source of data with regards to potentially sensitive topics of mental health difficulties (potential undiagnosed MDD or potential undiagnosed PTSD) and alcohol consumption. The veteran and LSC data on these variables were combined to identify the presence of a potential risk factor wherein if either the veteran or the LSC discussed the presence of a factor of interest it was deemed to be present.

### **Data Analysis**

Data were examined using descriptive analysis conducted using STATA statistical software V.15.0. Numbers and percentages are presented for categorical data and means (with standard deviations) or medians (with interquartile ranges) for continuous data. Univariable analyses methods were used including the  $\chi^2$  tests, Wilcoxon, Mann-Whitney U test, T-test and Fisher's exact test. Comparisons were made between those with a diagnosis of dementia and those without a diagnosis of dementia to identify any significant differences between the groups.

Please see the statistical terms glossary at the beginning of the report for more details on the statistics and statistical tests employed.

# Results

## Participants

121 participants are included in the final analysis reported: 48 cases (with a diagnosis of dementia) and 73 controls (without a diagnosis of dementia).

The demographic, military, lifestyle, medical and mental health characteristics of all veterans who participated in the study are described below. If

not specifically mentioned the outcome of interest refers to the status of the veteran at the time of the interview, for example their age at the time of interview. Any significant difference between the groups is shown in **bold, red text**. The type of statistical test used to generate the P value is in parentheses.

## Demographic factors

**Table One: Description of study participants demographic factors**

Factor of interest (number of participants)	No dementia diagnosis n (%)	Dementia diagnosis n (%)	P value (test)
Age group, years (120)			0.065 ( $\chi^2$ )
Up to 75	25 (35%)	7 (14%)	
From 75 up to 80	9 (13%)	8 (16%)	
From 80 up to 85	15 (21%)	15 (31%)	
From 85 up to 90	10 (14%)	13 (27%)	
Over 90	12 (17%)	6 (12%)	
<i>Mean (standard deviation)</i>	<i>80 (9.59)</i>	<i>82 (7.09)</i>	<i>0.132 (T-test)</i>
Relationship status at interview (120)			<b>0.008</b> ( $\chi^2$ )
Married/ in relationship	40 (56%)	38 (79%)	
Single (divorced, widowed)	32 (44%)	10 (21%)	
Number of children (119)			0.067 (Fisch.)
0	10 (14%)	4 (8%)	
1 or 2	42 (59%)	21 (44%)	
3 or more	19 (27%)	23 (48%)	
<i>Mean (standard deviation)</i>	<i>2.1 (1.27)</i>	<i>2.4 (1.22)</i>	<i>0.118 (T-test)</i>

$\chi^2$ : Chi Squared Test; Fisch.: Fischer's Exact Test

The majority of participants were aged between 80 and 85, were White British, married or in a relationship and had children. Participants in the dementia group were significantly more likely to be married or in a relationship compared to those in the non-dementia group who were more likely to be single (including divorced or widowed).

## Military factors

Table Two: Description of study participants military factors			
Factor of interest (number of participants)	No dementia diagnosis n (%)	Dementia diagnosis n (%)	P value (test)
Service branch (100)			<b>0.039</b> ( $\chi^2$ )
Naval services (including Royal Marines)	24 (39%)	6 (15%)	
Army	19 (31%)	17 (44%)	
Royal Air Force	18 (30%)	16 (41%)	
Rank (100)			0.406 ( $\chi^2$ )
Officer	23 (39%)	12 (31%)	
Non-commissioned officer	36 (61%)	27 (69%)	
Type of service (120)			<b>&gt;0.001</b> ( $\chi^2$ )
National service only	16 (22%)	21 (44%)	
Continued after national service	6 (8%)	13 (27%)	
Career service	50 (69%)	14 (29%)	
Length of service (97)			<b>0.021</b> ( $\chi^2$ )
Less than 3 years	6 (10%)	7 (18%)	
From 3 up to 10 years	16 (28%)	19 (49%)	
Over 10 years	36 (62%)	13 (33%)	
<i>Median (interquartile range)</i>	<i>14.75 (16.9)</i>	<i>5.5 (12.9)</i>	<b>0.028</b> (Wilc.)
Number of deployments (81)			0.143 (Fisch.)
0	11 (24%)	4 (11%)	
1	4 (9%)	7 (20%)	
From 2 up to 4	11 (24%)	13 (37%)	
5 or more	20 (43%)	11 (31%)	
<i>Median (interquartile range)</i>	<i>3 (7)</i>	<i>3 (5)</i>	0.8779 (Wilc.)
Combat exposure (108)			<b>0.007</b> ( $\chi^2$ )
No combat exposure reported	31 (46%)	29 (73%)	
Combat exposure reported	37 (54%)	11 (28%)	

$\chi^2$ : Chi Squared Test; Wilc.: Wilcoxon Mann Whitney U Test; Fisch.: Fischer's Exact Test

Those in the non-dementia group were more likely to serve in the Naval services (as opposed to Army or Royal Air Force) than those in the dementia group. Those in the dementia group were more likely to have only served in the military for national service (conscripted into military service for 2-3years), whereas those in the non-dementia group were more likely to have served as career soldiers (elected to join the Armed Forces and typically served for a minimum of 4 years). This also corresponded to a significantly shorter service length in the dementia group, and significantly lower rates of combat exposure in the dementia group but it did not result in significantly lower number of deployments when compared to the non-dementia group.

## Lifestyle factors

**Table Three: Description of study participants lifestyle factors**

Factor of interest (number of participants)	No dementia diagnosis n (%)	Dementia diagnosis n (%)	P value (test)
Educational level (117)			0.324 ( $\chi^2$ )
No or low qualifications (none or O levels)	23 (32%)	11 (24%)	
Mid-high qualifications (A levels – degree)	48 (68%)	35 (76%)	
Main occupation post service band (113)			0.964 ( $\chi^2$ )
Blue collar	25 (38%)	18 (38%)	
White collar	41 (62%)	29 (62%)	
Social activity (91)			0.707 ( $\chi^2$ )
No or low social activity*	20 (40%)	18 (44%)	
Medium or high social activity*	30 (60%)	23 (56%)	
Physical activity (117)			0.234 ( $\chi^2$ )
Physically active	64 (90%)	38 (83%)	
Physically inactive	7 (10%)	8 (17%)	
Smoking status (117)			0.874 (Fisch.)
Never smoked	24 (33%)	16 (36%)	
Used to smoke	43 (60%)	25 (56%)	
Currently smokes	5 (7%)	4 (9%)	
Potential alcohol abuse (112)			0.203 ( $\chi^2$ )
No alcohol abuse	43 (64%)	34 (76%)	
Potential alcohol abuse	24 (36%)	11 (24%)	
Overweight (119)			<b>0.001</b> ( $\chi^2$ )
Not obese or overweight	38 (54%)	40 (83%)	
Obese or overweight	33 (46%)	8 (17%)	

$\chi^2$ : Chi Squared Test; Fisch.: Fischer's Exact Test

*\*no/low social activity defined as limited social network with limited activity; medium/ high activity defined as group of friends and family with regular contact, numerous group memberships*

The majority of participants had A levels or above and had been in white collar roles since leaving the services (equating to 'managers, directors and senior officials', 'professional occupation', 'associate professional and technical occupation' and 'administrative and secretarial occupations'), with no significant differences between groups. Most participants were both socially and physically active post service and whilst most used to smoke, the majority no longer smoked. Only a small minority of participants reported having ever used illegal substances, for most of these experiences with illegal drugs were in their youth (marijuana, LSD, methamphetamine, opioids) although a small number reported currently using marijuana. Most participants did not demonstrate potential alcohol abuse, this was defined as either a diagnosis of alcohol abuse or self-reported alcohol consumption levels which exceeded recommended guidance. Weight status did differ significantly between the dementia and non-dementia group with those in the non-dementia group being significantly more likely to hold a diagnosis of obesity on their medical records or to self-report being overweight.

## Medical conditions

Table Four: Description of study participants medical conditions			
Factor of interest (number of participants)	No dementia diagnosis n (%)	Dementia diagnosis n (%)	P value (test)
Mild traumatic brain injury (120)			0.756 ( $\chi^2$ )
No mild traumatic brain injury	47 (65%)	30 (63%)	
Mild traumatic brain injury	25 (35%)	18 (38%)	
Cardiovascular conditions (91)			0.436 ( $\chi^2$ )
No cardiovascular conditions	16 (30%)	8 (22%)	
Cardiovascular conditions	38 (70%)	28 (78%)	
Metabolic syndrome (119)			<b>0.048</b> (Fisch.)
No metabolic syndrome	62 (87%)	47 (93%)	
Metabolic syndrome	9 (13%)	1 (2%)	
Hearing impairment (110)			0.608 ( $\chi^2$ )
No hearing issues	14 (22%)	12 (26%)	
Hearing issues	50 (78%)	34 (74%)	
Serious medical condition *(90)			0.707 ( $\chi^2$ )
No serious medical condition	37 (69%)	26 (72%)	
Serious medical condition	17 (31%)	10 (28%)	

$\chi^2$ : Chi Squared Test; Fisch.: Fischer's Exact Test

*\*includes cancer and epilepsy*

Around 35% of participants had experienced mild traumatic brain injury, less than 30% had experienced a serious medical condition (cancer or epilepsy), over 70% had experienced cardiovascular issues (hypertension, heart disease or stroke) and around 70% had experienced hearing issues. There were no significant differences between the dementia and non-dementia group for any of these factors. Between 2% (dementia) and 13% (non-dementia) had experienced metabolic syndrome (characterised as a combination of obesity, hypertension and diabetes), with the non-dementia group being more likely to experience metabolic syndrome. However, it is important to note that this difference was only in relation to the aforementioned difference in weight between the dementia and non-dementia group, with no difference seen for diabetes (dementia: 25% vs non-dementia: 26% p=0.921) or hypertension (dementia: 56% vs non dementia: 61% p=0.600) individually.

## Mental health conditions

Table Five: Description of study participants mental health			
Factor of interest (number of participants)	No dementia diagnosis n (%)	Dementia diagnosis n (%)	P value (test)
Ever: diagnosed or reported MDD or PTSD (120)			0.738 ( $\chi^2$ )
Absent	19 (26%)	14 (29%)	
Present	53 (74%)	34 (71%)	
In service: diagnosed or reported MDD or PTSD (120)			0.588 ( $\chi^2$ )
Absent	47 (65%)	29 (60%)	
Present	25 (35%)	19 (40%)	
Ever: diagnosed or reported PTSD (120)			0.769 ( $\chi^2$ )
Absent	38 (54%)	27 (56%)	
Present	33 (46%)	21 (44%)	
Ever: diagnosed or reported MDD (120)			0.820 ( $\chi^2$ )
Absent	30 (42%)	19 (40%)	
Present	42 (58%)	29 (60%)	
Benzodiazepine or psychotropic medication (90)			0.698 (Fisch.)
None	49 (91%)	34 (94%)	
Prescribed	5 (9%)	2 (6%)	

$\chi^2$ : Chi Squared Test; Fisch.: Fischer's Exact Test

There were no significant differences between the dementia and non-dementia groups regarding MDD or PTSD. This includes both a diagnosis of MDD or PTSD on their medical records or a report of potential mental health difficulties during the interview. This was true whether mental ill health was looked at as occurring across participants lifetime or divided into occurring during or post service.

The Cornell Depression Scale results demonstrate very low numbers of participants scored as a probable case for current depression and none scored for a definite case of current depression with no significant differences between the dementia and non-dementia groups.



# Discussion

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## Summary of results

This study examining the impact of mental ill health on the development of dementia in male military veterans over the age of 65 found no differences between the dementia and non-dementia group related to experience of mental ill health, which included both self-reported mental health difficulties and diagnosed mental health conditions. Service-related mental-ill health was not seen at a higher level in those with dementia when compared to those without dementia. Significant differences were found between the dementia and non-dementia group on a number of demographic, lifestyle and military risk factors.

With regard to demographic factors explored, the non-dementia group were more likely to be classified as not in a relationship. Relationship status is likely to be a good indicator of social activity, a low level of which is deemed to be a risk factor for dementia. As such one would expect not being in a relationship to act as a potential risk factor for dementia and therefore to be seen to a higher degree in the dementia group, not in the non-dementia group as found within this research.

For lifestyle factors, the non-dementia group were more likely to be obese or overweight. Again, being overweight in mid-life is typically thought of as one of the key modifiable risk factors for dementia, therefore we would expect to see this risk factor at a higher degree in the dementia group rather than the non-dementia group. However, examination of the research evidence supporting a relationship between obesity and dementia risk, suggests that whilst mid-life obesity appears

associated with an increased risk of dementia this affect may be reversed when examining late life obesity (Fitzpatrick et al., 2009; Loeff and Walach, 2012). Indeed, the term ‘obesity paradox’ has been used to explain the findings across a number of studies that indicate that a higher BMI in old age is associated with a lower risk of dementia. It is suggested that this reversal is seen because a low BMI in old age typically acts as an indicator for weight loss, frailty and perhaps even preclinical dementia as it has been shown to pre-date dementia by up to 10years (Fitzpatrick et al., 2009; Loeff and Walach, 2012). As our current study does not distinguish between mid and late life obesity we cannot say which is at play. It may be that the higher level of obesity in the non-dementia group relates to late life obesity (as opposed to mid-life obesity) which the current literature suggests should indeed be associated with a decreased risk of dementia.

Military factors demonstrate the greatest difference between the dementia group and non-dementia group across all factors explored. There were significantly more participants in the Naval Service in the non-dementia group when compared to the dementia group. This may be due to a range of factors related to service branch which we did not measure in this study.

The dementia group were significantly more likely to have who only served as part of national service, whereby they entered the Armed Forces as a result of compulsory conscription and served up to 3 years, in contrast to ‘career soldiers’ who joined the Armed Forces through choice and served for a minimum of 4 years. In line with this the dementia

group served for significantly less time than the non-dementia group and reported significantly less combat exposure (feeling that their own or others' lives were in danger). To summarise, the exploration of military factors suggests that those in the dementia group may have had a 'military light' experience wherein they had a shorter, less intense military experience more likely to relate only to national service when compared to those in the non-dementia group.

In each category of factors explored (demographic; lifestyle; medical; military) if any difference was seen, then those in the non-dementia group were more likely to be exposed to one or more risk factors for dementia. This is with the exception of the mental health related factors, where there were no differences between dementia and non-dementia group for any of the factors explored.

We noted that despite not having a higher lower exposure to known risk factors for dementia than those in non-dementia group, the dementia group still developed the condition. This suggests that another, as yet unknown, risk factor may be causing an increased risk for the dementia group or that the non-dementia group were subject to a protective factor which counteracted their potential for an increased risk for dementia.

### **Healthy soldier effect**

The healthy worker effect refers to those in employment being expected to exhibit lower levels of morbidity and mortality than the general population, since those who are unwell or unfit are less likely to enter into, and stay in, employment (Li and Sung, 1999). This healthy worker effect has been said to hold the potential to mask, at least partially, any increased risk of morbidity or mortality caused by harmful occupational exposures (Li and Sung, 1999).

The healthy worker effect would appear to hold particular resonance within a military population

in light of the rigorous fitness standards required for entry into the Armed Forces and the degree of enforced physical fitness required whilst serving. In addition to this, regular health screening that occurs as part of military service could result in medical conditions being identified, and treated, at an earlier time point potentially mitigating their possible harmful impact. Within the Armed Forces this effect has been labelled as the 'healthy soldier effect' (McLaughlin et al., 2008) regardless of which service an individual is a member of. The literature surrounding the 'healthy soldier effect' suggests that this effect equates to a reduction in mortality of between 10 and 25% when compared to the general population (McLaughlin et al., 2008).

Whilst the healthy soldier effect holds true for career service personnel, those who served in the Armed Forces as part of national service would not have been subject to the same degree of physical fitness at enlistment. All men between the ages of 18 and 51 were deemed eligible for national service but could then be rejected on medical grounds. Whilst this does ensure a degree of medical fitness it does not equate to the robust fitness procedures in place for entry into the Armed Forces outside of conscription. Rather than selecting the fittest of the population, this process simply ensured the unwell were not selected therefore representing a reduced level of fitness, and increased age, in those who joined via national service. In addition to this those who served as part of national service would have only been subject to enforced physical activity and enhanced health screening for a short period of time (up to 3 years).

In summary, those who join the military must demonstrate a high level of fitness, must continue to maintain a level of fitness and are privy to regular health screenings to detect and treat medical conditions early. These factors equate to a 'healthy soldier effect' which could mask occupational exposures which may increase the risk of dementia.

Further work is needed to compare military veterans with the general population in employment to unpick the impact of the healthy worker effect and dementia in military veterans. In particular, research which is able to exclude national service veterans, or include them as a distinctly separate group, would enable further exploration of the healthy soldier effect.

## **Comparison with existing military literature**

Evidence from the exploration of medical records in the US suggests that there is a relationship between both MDD and PTSD and later dementia, with both mental health conditions increasing the risk of developing dementia. The results of the current research do not support this relationship.

However, the research conducted in the US is based on medical records of those who utilise the Veterans Affairs (VA) service, the free healthcare service for veterans in the US. Those veterans who utilise the VA services are not a representative sample of US military veterans. They are more likely to have poorer health status, have more medical conditions, with lower levels of educational attainment, employment and income (Agha et al., 2000). The difference in results demonstrated between the US and UK military research fits into a wider trend whereby military veterans in the US appear to demonstrate a heightened degree of negative outcomes, including higher rates of PTSD (Sundin et al., 2014).

## **Strengths**

This research is the first of its kind to explore the relationship between mental health conditions and dementia in the UK military veteran population. As such it represents an important first step in exploring the potential risk associated with mental conditions and the later development of dementia.

In addition to extracting variables of interest from medical and military records this research employed in-depth interviews with both veterans and their long-standing companions to provide a more granular inspection of both veterans mental health and other lifestyle, medical and military factors of interest.

## **Limitations**

Research from the US based on medical record extraction is conducted on large numbers of participants. To enable the level of detail gathered from interviews the current research was unable to utilise comparably large participant numbers.

The results of the research appear to be affected by the large number of military veterans who served in the Armed Forces as part of National Service. It is suggested that these military veterans had a distinctly different experience of the military when compared to career soldiers. Unfortunately, within the age range of veterans utilised for this research a large proportion served via National Service representing a significant challenge to recruitment if this group were to be excluded from the research.

## **Future research**

This study did not identify PTSD or MDD as risk factors for dementia within UK military veterans. This finding is at odds with other results from other nations. We suggest that a more powerful, large-scale, cohort study is needed to assess UK military veterans' MDD/ PTSD and dementia status over a significant period of time, including the capturing of neurobiological markers and the use of brain imaging to examine this important topic in more detail and to understand the mechanisms underlying any association found. Such studies should allow for comparisons between national service veterans, career service veterans and the general public in order to provide an exploration of the impact of the healthy soldier effect on the development of dementia in military veterans.

# Conclusion

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Service-related mental ill health and dementia do not appear to be related in the sample of UK military veterans explored within this research. There was no difference in the level of mental health difficulties reported in those veterans with dementia when compared to those veterans without dementia.

However, those veterans in the dementia group were more likely to have only experienced military service as part of national service, where in they were conscripted to military service for a period of up to 3 years. The dementia group were more likely to have served in the military for less time and reported lower levels of combat exposure.

The development of a dementing illness seen in the dementia group, but not in the non-dementia group despite heightened levels of obesity and single relationship status, may be explained by the higher level of national service seen in the dementia group.

Those who served in the military as their career, rather than only completing national service, are represented to a higher degree in the non-dementia group could be subject to the 'healthy soldier effect' wherein the heightened level of physical fitness of the Armed Forces may mask the potential harmful exposures on the risk of developing dementia in later life. We suggest that when all the relevant risk factors are considered, our data support career military service, but not national service, as a protective factor for dementia.

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