COHORT PROFILE

Profile of two cohorts: UK and US prospective studies of military health

Richard J Pinder,^{1†} Neil Greenberg,¹*[†] Edward J Boyko,² Gary D Gackstetter,³ Tomoko I Hooper,⁴ Dominic Murphy,¹ Margaret AK Ryan,⁵ Besa Smith,⁶ Tyler C Smith,⁶[‡] Timothy S Wells⁶ and Simon Wessely^{1‡}

¹King's Centre for Military Health Research and Academic Centre for Defence Mental Health, King's College London, Institute of Psychiatry, Weston Education Centre, London, UK, ²Seattle Epidemiologic Research and Information Center, Department of Veterans Affairs Puget Sound Health Care System, Seattle, WA, USA, ³Analytic Services, Inc. (ANSER), Arlington, VA, USA, ⁴Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda, MD, USA, ⁵Naval Hospital Camp Pendleton, CA, USA, ⁶Department of Deployment Health Research, Naval Health Research Center, San Diego, CA, USA

*Corresponding author. King's Centre for Military Health Research and Academic Centre for Defence Mental Health, King's College London, Institute of Psychiatry, Weston Education Centre, Cutcombe Road, London, UK. E-mail: sososanta@aol.com [†]These authors contributed equally to this work

[‡]These authors are joint senior authors

Accepted 18 May 2011

How did the studies come about?

The importance of military health

Since 1980 with the introduction of the diagnosis of post-traumatic stress disorder (PTSD) in the Diagnostic and Statistical Manual of Mental Disorders. Third Edition (DSM-III), the long-term consequences of psychological trauma have gained more widespread recognition.1 Subsequently, the 1991 Gulf War controversies²⁻⁵ and, more recently, an evolving public focus on negative health outcomes related to combat in Iraq and Afghanistan^{6,7} catalyzed the need for a systematic analysis of the physical and psychological well-being of military service personnel. This, together with societal pressures, including public interest, a changing legal climate, spiralling healthcare costs and the military necessity of maintaining a healthy workforce in a high operational tempo climate, led to the design and implementation of prospective cohort studies of military populations in both the UK and the USA.

In the UK and USA, these two independent cohort studies have been instituted to prospectively study the health of service personnel and veterans. From comparisons with baseline information, these studies are designed to better inform the military and the public on how best to protect the health of their armed forces and better understand the long-term risks of some occupational exposures that extend beyond military communities. In order to do this, these studies consider:

- (i) The underlying physical and mental health of the military populations before, during and after military service.
- (ii) The specific effects of deployment, deploymentrelated exposures and other occupational exposures upon personnel compared with unexposed subgroups.

Whereas previous studies have attempted to address these topics, they have often been limited in their generalizability to all service branches and components of the military, or previous population-based methodologies have been largely limited to cross-sectional or retrospective methods.^{3,6–10} Follow-up to the National Vietnam Veterans Readjustment Survey,⁹ called the National Vietnam Veterans Longitudinal Study, is still ongoing,¹¹ but it is focused on a single deployment. Similarly, the Air Force Health study, a 20-year longitudinal study of approximately 20000 Vietnam veterans, assessed potential health effects associated with exposure to aerial spraying of dioxins.¹² Here, we present two prospective, longitudinal, multi-service studies of active duty and Reserve/National Guard personnel that will continue to follow participants even after they have left military service.

We describe these two studies in detail, comparing study populations, methodology and the published literature so far. Potential areas for future collaboration are also explored. By understanding the inherent similarities and differences between these two cohorts and leveraging each study's unique strengths and strategies to minimize limitations, we aim to analyse, inform and ultimately improve the health of both nations' military personnel and extend findings to non-military populations with similar occupational concerns.

King's Centre for Military Health Research

The King's Cohort (UK)

Beginning in 1996 as the Gulf War Illnesses Research Unit, the King's Centre for Military Health Research (KCMHR) was formally established in 2003 with funding from the UK Ministry of Defence (MoD) as an independent multi-faculty research centre within King's College London. Its express aim is to assess the health of the British Armed Forces and veterans.

Since 2003, KCMHR has begun a wide-ranging dynamic prospective cohort study of the physical and psychological health of more than 10 000 personnel serving at the time of the Iraq War.¹³ More recently, the cohort expanded to include a new sample of those who had served in Afghanistan and those who had joined the UK Armed Forces since 2003.

The Department of Defense, Center for Deployment Health Research

The Millennium Cohort (USA)

In 1998, the US Department of Defense (DoD) reported a need to determine whether exposures during deployment affected post-deployment military health.⁴ Moreover, in 1999, the Institute of Medicine recommended a need for a broader population-based study to collect long-term information on the health of the US Armed Forces, both while serving and after separation.¹⁴ From late 1999, these needs were satisfied by the development of an expert taskforce encompassing all service branches, the DoD and the Department of Veterans Affairs (VA), with the explicit aim of establishing a comprehensive, long-term systematic study.

The Millennium Cohort Study,¹⁵ begun in 2001, will ultimately follow a population-based cohort of approximately 200 000 uniformed personnel from the Army, Navy, Air Force and Marine Corps, including active duty, Reserve and National Guard forces, to determine if factors related to military service are associated with any long-term health outcomes.

Funding

KCMHR, based at King's College London, is funded primarily by the UK's MoD. However, the MoD recognized the need to have independent researchers investigating important issues, and thus it has no role in the design, analysis, interpretation or decision to submit work for publication. Researchers have full access to the data in published work, and have the final responsibility for the decision to submit for publication.

The Millennium Cohort Study, based at the Department of Deployment Health Research, Naval Health Research Center, San Diego, CA, is a multi-service and multi-agency team effort. Study investigators, including senior officers from the US Army, Navy, and Air Force and senior civilians from the VA and DoD participate in questionnaire design, analysis plans, interpretation of results and preparation of manuscripts for publication, as well as overall strategic planning. Collaborators from civilian academic institutions participate in nearly all analysis projects. The Millennium Cohort Study is funded by the US DoD through the US Army Medical Research and Materiel Command, Military Operational Medicine Research Program. The Millennium Cohort Study strategic research plan is guided by the team of investigators who prioritize and conduct studies relevant to the DoD, the VA or are otherwise important to the health of the general US population.

The strategic research plan and study progress are reviewed by independent expert panels, including the American Institute of Biological Sciences, the Defense Health Board and the Millennium Cohort Study, Scientific Steering Committee. In addition, this study was approved by the Naval Health Research Center, Institutional Review Board.

What do the cohort studies encompass?

Survey content

Both the King's Cohort and Millennium Cohort data sets collect data concerning demography; service history; occupational exposures, with special focus on deployment-related exposures; experiences postdeployment; behavioural characteristics, such as alcohol and tobacco use; and current and past physical and mental health.

Survey modes

The King's Cohort uses a 28-page, 143-question booklet, which includes information about the voluntary nature of participation in the study and the independence of the MoD research team and requests consent to be contacted for follow-up.^{10,13} The methods of contact are multi-faceted: initially, research team members introduced the study to military personnel together with a mail-out; non-responders were followed up twice via repeated mailings of the questionnaire.¹³ To determine response bias, 150 individuals were identified for intensive follow-up with civilian and military tracing.¹⁶ No evidence of response bias was found in terms of the principal outcomes.¹⁶ First-round data were collected from March 2004 until March 2006, retrospectively determining whether participants had deployed in March 2003 on Operation Telic 1. Telic is the code name for UK operations in Iraq, and is the counterpart to the US Operation Iraqi Freedom. A further follow-up is currently being conducted to include personnel deployed to Afghanistan (Operation Herrick; UK counterpart to US-named Operation Enduring Freedom) as well as personnel who have joined since 2003, and to further replenish the cohort, with results published in May 2010.¹⁷

The Millennium Cohort collects data through both traditional paper-based techniques as well as an online version of the questionnaire.^{15,18–20} Consent is obtained through paper or online processes.¹⁹ The Millennium Cohort survey is 24 pages in length and includes more than 450 questions. Invitations or requests for follow-up are initially sent through e-mail contact to encourage online survey submission and are followed by US Postal Service mailed introductory postcards, paper surveys and subsequent reminder postcards based on a modified Dillman approach.²¹ Data were collected for the first enrolment panel, from July 2001 to June 2003, beginning prior to the onset of military conflicts in Iraq and Afghanistan. The first 3-year follow-up and enrolment of a new accession cohort was conducted between June 2004 and February 2006. A second follow-up of the first panel, a first follow-up of the second panel and enrolment of a new accession panel were conducted from June 2007 to December 2008. The follow-up cycle of all three panels, including more than 150 000 cohort members, will also include an additional accession panel of 60 000 with a family component which launched in May 2011.

Who are the cohort participants?

For the King's Cohort, the Defence Analytical Services and Advice (DASA) identified personnel in all branches (excluding special forces and high security personnel) who deployed to Operation Telic 1 and those who did not, but were present in the UK Armed Forces on 1 March 2003. These two populations were stratified by service and enlistment type (regular or reserve), and a random stratified sample was selected from both populations, totalling 17698 individuals. Because of particular concerns in the UK about the effects of deployment on reservists, the King's Cohort oversampled reservists by a ratio of 2:1. The total sample represents 4.6% of the serving UK Armed Forces. Of the 17698 individuals identified by DASA, 10272 consented to participate and returned questionnaires (58.7%), and were included in the study. A comparison of responders and non-responders showed bias due to non-response to be small and that increasing the response rate had little effect on the results;¹⁶ non-response was not

influenced by health status (as assessed by objective data on medical downgrading) but instead followed the familiar pattern of being associated with single and enlisted young men.¹³

Follow-up is currently of the initial King's Cohort,¹⁷ and is complete with all those who consented to follow-up being contacted; in cases of non-response intensive tracing through civilian and military channels was employed.¹⁷ Address data and vital status are updated periodically via DASA. The cohort has also been supplemented with two further groups: the first comprised individuals deployed to Afghanistan over a 12-month period from April 2006, and the second included a replenishment sample comprising personnel who joined the military since the initial sample was recruited in 2003.¹⁷

For the Millennium Cohort, the Defense Manpower Data Center (DMDC) identified personnel in all branches of the military listed on service rosters as of 1 October 2000.

A probability-based sample was then selected, with oversampling of Reserve and National Guard members, previous deployers and women, to ensure adequate power for statistical inferences in these smaller subgroups of the military.¹⁵ The total sample represents approximately 11.0% of those on service rosters as of 1 October 2000. Of the 256 400 individuals identified by DMDC, because of the sudden increase in operational tempo as a result of the terrorist attacks on 11 September 2001, slightly more than 214 000 eligible personnel were able to be located and contacted, and 77047 consented to participate and returned questionnaires (36.0%).¹⁸ To facilitate follow-up, participants are able to amend their address details using the Millennium Cohort website. Where there is no response to follow-up, the US Postal Service, Social Security Administration and Internal Revenue Service can be used for tracing. Vital status is updated prior to each survey cycle and is obtained from the National Death Administration Index. Social Security Death Master File, Department of Veterans Affairs files and the Department of Defense Medical Mortality Registry.

Additional panels of 31110 and 43400 individuals from population-based samples obtained in 2004 and 2007 respectively, were enrolled; these panels used similar sampling strategies to those of the first panel, but were limited to new accessions (1–3 years of military service), adding oversampling of Marine Corps personnel and eliminating oversampling of those previously deployed. Analyses to investigate potential reporting biases show minimal differences in responder health with respect to hospitalization and outpatient encounters in the year prior to enrolment,²² strong test–retest reliability,²³ reliable immunization reporting²⁴ and deployment reporting,²⁵ minimal differences between participants choosing online submission in comparison with paper submission¹⁹ and cohort members' representativeness of the overall US military.¹⁸

Despite differences in recruitment criteria, proportion of military sampled, size of the cohorts, timing of initial baseline enrolment and response rates, as well as factors related to differences in military structures between the two countries (e.g. inclusion of the US Coast Guard and higher number of officers and women for the USA), these cohorts demonstrate similar characteristics for predictors of baseline and follow-up response rates.

In comparing the two cohorts, there is a major difference related to the timing of initiation. The Millennium Cohort began enrolment prior to 11 September 2001 and the start of the conflicts in Iraq and Afghanistan. However, both cohorts cover the main period of counterinsurgency operations in Iraq.

The most reasonable time frame for directly comparing the two cohort studies, particularly with respect to the contingency operations in Iraq and Afghanistan, involves the initial enrolment of the King's Cohort with the first follow-up phase of the Millennium Cohort (Figure 1). In relation to the analysis of the effects of deployment on military personnel, again the two cohorts can be separated into deployed and non-deployed groups (Figure 2). Of note is the distinction of how deployment is defined: whereas the King's Cohort specifies whether personnel have deployed to Iraq, the Millennium Cohort includes and distinguishes deployments in support of the operations in Iraq, Afghanistan and other countries in those regions, and importantly defines whether such deployments included exposure to combat-related stressors.

What information is being collected and what health outcomes are measured?

Demographics and service history

Follow-up

 $(n = 50\ 020)$

Not Deployed

 $(n = 28\,690, 52.1\%)$

Deployed

 $(n = 26\,330, 47.9\%)$

Demographic data and service history were collected in both studies. Data obtained from personnel files

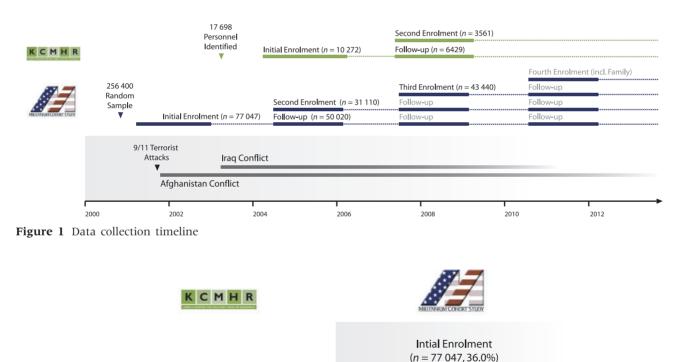


Figure 2 Sample selection for direct comparison^{13,15,37}

Deployed on TELIC

(n = 4722, 46.0%)

Initial Enrolment

 $(n = 10\ 272, 58.7\%)$

Not Deployed on TELIC

(n = 5550, 54.0%)

include sex, age, marital status, educational level, service branch, occupation, service status (active, regular or reserve), rank and service history, including deployment. In addition to these data collected by both studies, the Millennium Cohort also routinely collects electronic data kept within the US Military Health System, including inpatient and outpatient encounters, pharmacy transactions and vaccinations administered.

Further analysis within the Millennium Cohort comparing objective records with self-reported data showed a substantial level of agreement,^{25,26} and no difference in health status for those who reported their immunizations, deployment status and occupation.^{24–27} Therefore, we can assume that the differences related to data collection methods are minimal.

General health and psychological morbidity (including service exposures)

A comparison of questionnaire domains and instruments is provided (Table 1).

In the general, for assessment of psychological health and functional status domains, the King's Cohort uses the General Health Questionnaire 12 (GHQ-12)²⁸ and multiple physical symptom score,¹³ whereas the Millennium Cohort uses the Patient Health Questionnaire (PHQ)²⁹ in addition to the more expansive Medical Outcomes Study Short Form 36-Item Health Survey for Veterans.³⁰ Broad comparison between the GHQ and PHQ may be possible²⁸ via comparison of baseline prevalence of likely psychological morbidity. In a more recent follow-up of a subgroup of the King's Cohort, the PHQ has been used for an additional 813 participants,³¹ which will allow direct comparisons with the Millennium Cohort.

The PTSD Checklist-Civilian Version $(PCL-C)^{32}$ is used in both studies, although to date the two cohorts have applied and published different criteria: the King's Cohort has used the PCL-C with a score ≥ 50 , whereas the Millennium Cohort has applied these criteria in addition to more specific criteria (i.e. presence of one intrusion symptom, three avoidance symptoms and two hyperarousal symptoms as defined by the DSM-IV).³³

The fatigue score used in the King's Cohort at its inception was intended for direct comparison against a previous Gulf War cohort¹⁰ and was not intended for widespread comparison; this measure was not

Domain	King's Cohort	Millennium Cohort
Demographics	Sex, age, marital status, educational level, service, status, rank and service history	Sex, age, marital status, educational level, service, status, rank and service history
General health including psychological morbidity	General Health Questionnaire 12 (GHQ-12) ²⁸ Multiple physical symptom score ¹³ Fatigue score ¹³ Body mass index (BMI)	Patient Health Questionnaire (PHQ) (self-administered Primary Care Evalua- tion of Mental Disorders, PRIME-MD) ²⁹ Medical Outcomes Study Short Form 36-Item Health Survey for Veterans ³⁰ BMI History of head trauma Physical activity Alternative medicine usage Previous stressful life events
PTSD	PTSD Checklist-Civilian Version (PCL-C) ³²	PTSD Checklist-Civilian Version (PCL-C) ³²
Substance use	Alcohol Use Disorders Identification Test (AUDIT) questionnaire ³⁴ Tobacco history	CAGE questionnaire ³⁵ PHQ ²⁹ Tobacco history
Military exposures	Occupational exposures: fumes/oil smoke/ asbestos/chemicals/lasers/depleted uran- ium/insecticides Deployment-specific exposures: discharged weapon in direct combat/thought might be killed/came under fire/hostility from civilians/witnessing personnel killed or wounded/handled bodies/aided wounded. ¹³ Vaccination history	Department of Veterans Affairs Gulf War Survey of specific war-time exposures ^{3,5} Occupational exposures: hazards necessi- tating personal protective equipment/ paints and solvents/depleted uranium/ microwaves/pesticides Deployment-specific exposures: danger of being killed/attacked/ambushed/clearing homes/IED/wounded/dead bodies/know- ing someone seriously wounded or killed/seeing seriously injured or killed/ responsible for death of combatant or non-combatant ³⁷ Vaccination history

 Table 1
 Questionnaire domains and validated instruments

used in the follow-up. Although these data are not directly comparable, the Millennium Cohort includes a list of 19 symptoms based on previous Gulf War studies³ and also includes the PHQ assessment of somatic symptom disorder.²⁹

Alcohol scores are not directly comparable since the King's Cohort used the Alcohol Use Disorders Identification Test (AUDIT)³⁴ and the Millennium Cohort used the CAGE questionnaire³⁵ as screens for potentially harmful alcohol consumption. However, the Millennium Cohort was also able to use the PHQ²⁹ score to further assess possible alcohol misuse (alcohol-related problems), and other alcohol questions assessed usual quantity of alcohol consumed and binge drinking. Tobacco use was recorded in both questionnaires. The Millennium Cohort, unlike the King's Cohort, assessed alternative medicine usage, physical activity, occupation, head trauma, previous stressful life events, service satisfaction and separation from military service.

Although there were some differences in the range of questions about military exposures in the two studies, there are enough similarities that some degree of comparison should be possible. Vaccination histories were obtained in both studies.

What are the participation and attrition rates?

Response rates differ markedly between the two studies (Table 2). The reasons for non-response in the King's Cohort are presented elsewhere.^{13,17} For the Millennium Cohort, non-response rates reflect nonresponse among those who were able to be contacted, and therefore individuals lost to follow-up or dead are not included. Review of data for both studies has shown minimal response bias.^{16,22}

What has been found so far?

Demographics

Considerable differences exist demographically between the two cohorts (Table 3). However, these

Table 2 Comparison of attrition rates

Stage	King's Cohort n (%)	Millennium Cohort n (%)	
Recruitment			
Invitations	17 598	214 388	
Complete questionnaire	10272 (58.4)	79266 (37.0)	
Included in the study	10272 (58.4)	77 047 (35.9)	
Stage 1 follow-up			
Invitations	17812	77 047	
Complete questionnaire	9990 (56.1)	50 020 (64.9)	

largely reflect the underlying populations sampled and the results of oversampling some subgroups by design. This is highlighted in the proportions of personnel deployed. In each sample, the Army is proportionally the largest service branch, both deployed and non-deployed, followed by the Air Force and then Navy and Marine Corps.

The largest differences are apparent in the age distributions of these cohorts: the UK cohort is considerably younger, with approximately 15-20% born after 1979, in contrast to 5% born in this era in the US cohort. This sample differs from previous papers that showed an older deployed UK force.⁶ The age differential partly explains the difference in educational attainment levels, which is also reflected in the higher proportion of commissioned officers and health-care professionals in the US cohort. Underlying differences in the availability of military scholarships and differing education systems between countries may be additional factors influencing demographics of the two study populations.

Exposures

In view of concerns over specific military exposures, psychological and physical, both studies gathered data on exposure to traumatic experiences, chemical compounds, ordinances, military-specific vaccines and other possible health-related exposures, such as insect repellent.

Even though the questions were not directly comparable in all instances, there are some areas of overlap (Table 4) and potential for comparison.

Psychological health and PTSD scores

King's Cohort data distribute psychological morbidity outcomes to common mental disorders, PTSD, fatigue case, multiple physical symptoms, case on AUDIT and a rating of 'fair or poor' general health.¹³

Previously published data from KCMHR suggest an underlying 20% prevalence of common mental disorders (as identified by GHQ-12 score), and 13% prevalence of suspected alcohol misuse (based on AUDIT screen).³¹ The PTSD prevalence was reported at 4% overall (defined as PCL-C \geq 50), with no difference between those deployed on TELIC 1 (adjusted odds ratio 1.00, 95% confidence interval, 0.79–1.28).¹³

Millennium Cohort data, on the basis of the PHQ, provide a more detailed breakdown of common mental disorders into major depressive disorder, panic syndrome, other anxiety disorder, somatoform disorder, alcohol misuse and eating disorder, in addition to PTSD.

Data from the Millennium Cohort initial sample PHQ breakdown indicated the following prevalences: depressive disorder (3.2%), panic syndrome (1.0%), other anxiety syndrome (2.0%), alcohol misuse (12.6%) and eating disorder (3.1%).³⁶ PTSD

	King's	Cohort	Millennium Cohort follow-up*	
	Deployed $n = 4722$ (%)	Not deployed $n = 5550$ (%)	Deployed $n = 16785$ (%)	Not deployed $n = 38235$ (%)
Sex				
Male	4290 (90.9)	4949 (88.5)	13 763 (82.0)	26 585 (69.5)
Female	432 (9.1)	601 (11.5)	3022 (18.0)	11 650 (30.5)
Year of birth				
Before 1960	360 (7.6)	740 (13.3)	2760 (16.4)	10719 (28.0)
1960–69	1437 (30.4)	1908 (34.4)	6909 (41.2)	15 398 (40.3)
1970–79	1994 (42.2)	2020 (36.4)	6212 (37.0)	20739 (54.2)
1980 and later	931 (19.7)	882 (15.9)	904 (5.4)	1379 (3.6)
Education				
High school or equivalent	3661 (77.5)	4047 (73.8)	12382 (73.8)	26248 (68.6)
Degree or above	780 (16.5)	1156 (20.8)	4403 (26.2)	11 987 (31.4)
Service				
Navy/Marine corps/Coast	761 (16.1)	915 (16.5)	3058 (18.2)	9169 (24.0)
Guard	3066 (64.9)	3536 (63.7)	7791 (46.4)	18478 (48.3)
Army	895 (19.0)	1099 (19.8)	5936 (35.4)	10588 (27.7)
Air force				
Status				
Regular	3936 (83.4)	4750 (85.6)	10 684 (63.7)	20214 (52.9)
Not regular	786 (16.6)	800 (14.4)	6101 (36.3)	18021 (47.1)
Enlistment type				
Officer	814 (17.2)	1138 (20.5)	4247 (25.3)	10655 (27.9)
Enlisted	3908 (82.8)	4412 (79.5)	12 538 (74.7)	27 580 (72.1)
Service type				
Combat	1091 (23.1)	1306 (23.5)	4094(24.4)	7130 (18.6)
Service and support (not health care)	3142 (66.5)	3867 (69.7)	11 552 (68.8)	26 083 (70.1)
Health care	420 (8.9)	299 (5.4)	1139 (6.8)	5022 (13.1)

Table 3 Comparison of cohort demographics and service history

*Deployment status ascertained only between the baseline and first follow-up survey.

prevalence in the baseline Millennium Cohort survey was reported at 2.4%, based on the more specific DSM-IV criteria.³⁶ The total prevalence of any mental disorder based on the PHQ and PTSD combined is 18.3% and is broadly comparable with the King's data (20.0%).

Millennium Cohort data collected between 2001 and 2003 applied more specific criteria combining DSM-IV criteria with PCL score \geq 50 for a likely diagnosis of PTSD.³⁷ A likely diagnosis was reported in 7.6% of cohort members who were deployed and self-reported combat exposures, 1.4% of cohort members who were deployed and did not self-report combat exposures, and 2.3% of non-deployed cohort members. Because of differences in reporting combat exposures, a direct comparison between the Millennium Cohort and the King's Cohort is difficult, although the most recent King's data suggested that approximately 7% of

combat troops reported symptoms consistent with a diagnosis of PTSD; however, this figure relates to prevalence rather than incidence.

What are the main strengths and limitations?

These two cohort studies stand alone as the only large-scale, population-based, prospective cohort studies that include all branches of the military as well as veterans, and collect primary data directly from study subjects. Previously disparate studies have attempted to quantify the burden of PTSD and other disorders; reported prevalence has been markedly diverse largely because of differences in sampling and study methodology.^{38,39} Consistent application of methods and measurements, as is possible in these

King's Cohort Question	Millennium Cohort follow-up ³⁶ Question		
Composite: saw UK/allied forces/enemy forces/civilians killed or wounded	Ever witnessed a person's death due to war, disaster or tragic event		
Composite: came under hostile fire Composite: handled bodies Composite: provided aid Thought might be killed	Exposed in past three years to any exposure physical or psychological during a military deployment that had a significant impact on your health Danger of being killed/attacked/ambushed/clearing homes/ improvised explosive device/wounded/dead bodies/ knowing someone seriously wounded or killed/seeing seriously injured or killed/responsible for death of combatant or non-combatant ³⁷		
	Ever exposed to chemical or biological warfare agents		
Anthrax vaccine	Exposed to anthrax vaccine Exposed to smallpox vaccine		
Composite: Handled/inhaled/entered vehicles destroyed by depleted uranium	Exposed in past 3 years to depleted uranium		
	Exposed in past 3 years to occupational hazards requiring protective equipment		

Table 4	Comparison	of military	exposure	variables
---------	------------	-------------	----------	-----------

two cohort studies, will improve findings and, for the first time, provide better estimates of the true health effects of military service.

However, since these are both studies of the military and largely reliant upon self-reported data, they are subject to the biases associated with studies of this kind. Given the stigma attached to mental disorders, particularly within military populations, these conditions or symptoms may be under-reported, both because of unique sociocultural circumstances, and legal and medical fitness-for-duty issues. The use of standardized and validated screening instruments as a surrogate for a clinician diagnosis may misclassify PTSD status for some participants; however, self-reported survey data may be better measures of the magnitude of the disorder than ambulatory or hospitalization data since those with PTSD symptoms may not seek health care owing to stigma and other barriers.

Military populations present challenges to researchers, particularly in a longitudinal study, because they are highly mobile, frequently deployed, and are, for the most part, composed of young single men, an epidemiologically difficult group to canvas. Moreover, military populations may well be healthier than their civilian equivalents.³⁹ Part of this difference is due to health screening prior to entry, as well as a preponderance of younger age groups, universal access to health care, full employment and social support structures derived from the nature of their military employment.

Although the aforementioned strengths and limitations apply to both military populations, exact comparisons of the two are complicated by differences in structures such as command structures, and differing military priorities at home and overseas. These differences, however, can lead to research opportunities. By comparing and contrasting the manner in which each military organization sets up and runs its operations and support services, inferences can be drawn about the effects of differing structures and processes (e.g. the regimental system of the British Army or the length of overseas combat deployment for the US military). Another core difference lies in the health-care delivery systems for veterans and military members. In the USA, service members have access to the Military Health System while in active service, whereas the VA, a separate government agency for veterans, exists to provide care to US veterans after separation from military service. There is no equivalent in the UK since all veterans have access to the same level of health care as the general population as part of the National Health Service.

As contingency operations continue, the pool of personnel who have not deployed will decrease, which could potentially affect the non-deployed comparison groups used for investigation of post-deployment health outcomes. In the Millennium Cohort, enrolment of additional samples, composed of individuals with 1–3 years of active service, has helped to mitigate this potential limitation. It has similarly been valuable to define deployment-specific exposures in the Millennium Cohort, such that deployed unexposed members serve as the appropriate comparison group for many analyses.

Specifying the exact nature or role of the armed forces within the theatre of operations is difficult; the complexity of roles varies from service to service, as well as from theatre to theatre. This type of information is very difficult to capture using a questionnaire, even with access to non-classified military records, and even more difficult to meaningfully quantify for analysis. That said, as operations continue across the theatres of war with personnel facing similar hazards in similar roles, there will likely be further opportunities to compare and contrast experiences between the two cohorts that have not been apparent previously. The improved ability to capture and quantify in-theatre exposures will be critical in better differentiating deployment experiences in the context of their impact on health outcomes.

Scope for collaboration

Given the population-based samples and scope of both studies and the areas of overlap that we have described, there is an abundance of themes on which collaboration may inform and enhance both the practice and management of military health. Considerable common ground already exists for the analysis of PTSD and other common mental disorders, as well as more specific areas such as vaccination use,^{26,40–43} the health effects of combat and military service^{44,45} and publications on research methodology.^{16,19,25,46,47}

That is not to say that collaboration should be restricted to the analysis of previously collected data sets. Since both cohorts are prospective and ongoing, there may be appropriate areas for possible alignment of data collection efforts for future follow-up surveys.

Of increasing interest and value-added potential is the integration of complementary data sources,²⁰ such as objective military records, health records and personnel databases, which is already possible through the US DoD and actively used by the Millennium Cohort Study.²⁰ Despite hurdles caused by data protection laws in the UK,⁴⁸ the King's Cohort has already accessed a number of sources, including the Operational Emergency Department Attendance Register, which captures information on treatment for those attending emergency medical facilities, the Police National Database and information on whether personnel are medically fit to deploy.

New perspectives and the harnessing of inherent differences between the two studies can provide unrivalled opportunity to improve the health of both militaries. For example, in the case of alcohol misuse, the comparison of policy between the two countries may identify best practices and stimulate policy improvement. The opportunity to compare and contrast these two military cohort studies presents us with the possibility of adding substantial value to the initial concept and potential of both endeavours. Despite the aforementioned differences and limitations in methodologies, analyses of these two cohorts provide the prospect of driving improvement and innovation in military health and extending findings to other occupational populations.

Can I have access to the data?

Due in part to the military nature of the cohorts, opportunities for external investigators to share de-identified data from either cohort are limited and subject to ethical approval. Applications should be made to kcmhr@kcl.ac.uk and milcohortinfo@med.navy.mil for the King's Cohort and Millennium Cohort, respectively.

Funding

The King's Centre for Military Health Research and Academic Centre for Defence Mental Health are funded by the UK Ministry of Defence. The authors work was independent of the UK Ministry of Defence, which had no role in the analysis, interpretation or decision to submit this paper. The authors disclosed the paper to the Ministry at the point of its submission for publication. R. J. Pinder is funded as an academic clinical fellow by the National Institute for Health Research (NIHR) Integrated Academic Training Programme. S. Wessely is partially funded by the South London and Maudsley NHS Foundation Trust/ Institute of Psychiatry NIHR Biomedical Research Centre. The Millennium Cohort Study: This work represents report 11-12, supported by the Department of Defense, under work unit no. 60002. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of the Army, Department of the Air Force, Department of Defense, Department of Veterans Affairs or the US Government. Approved for public release; distribution unlimited. This research has been conducted in compliance with all applicable federal regulations governing the protection of human subjects in research (Protocol NHRC.2000.0007).

Acknowledgements

We are indebted to the Millennium Cohort Study participants, without whom these analyses would not be possible. In addition to the authors, the Millennium Cohort Study Team includes Paul J. Amoroso, MD, MPH (Madigan Army Medical Center, Fort Lewis, WA); Gregory C. Gray, MD, MPH (College of Public Health and Health Professions, University of Florida, Gainesville, FL); and James R. Riddle, DVM, MPH (retired from the Air Force Research Laboratory, Wright-Patterson Air Force Base, OH). We thank Melissa Bagnell, MPH; Nisara Granado, MPH, PhD; Jaime Horton; Isabel Jacobson, MPH; Kelly Jones; Cynthia LeardMann, MPH; Travis Leleu; Jamie McGrew; Amanda Pietrucha, MPH; Teresa Powell, MS; Donald Sandweiss, MD; Amber Seelig, MPH; Katherine Snell: Steven Speigle: Kari Sausedo, MA: Martin White, MPH: James Whitmer: and Charlene Wong, MPH; from the Department of Deployment Health Research, Naval Health Research Center, San Diego, CA, USA. We thank Scott L. Seggerman from the Management Information Division, Defense Manpower Data Center, Seaside, CA, USA. We also thank all the professionals from the US Army Medical Research and Materiel Command, especially those from the Military Operational Medicine Research Program, Fort Detrick, MD. We appreciate the support of the Henry M. Jackson Foundation Advancement of Military for the Medicine. Rockville, MD.

Conflict of interest: None declared.

References

- ¹ Jones E, Wessely S. A paradigm shift in the conceptualization of psychological trauma in the 20th century. *J Anxiety Disord* 2007;**21**:164–75.
- ² Ismail K, Everitt B, Blatchley N *et al.* Is there a Gulf War syndrome? *Lancet* 1999;**353**:179–82.
- ³ Gray GC, Reed RJ, Kaiser KS, Smith TC, Gastanaga VM. Self-reported symptoms and medical conditions among 11,868 Gulf War-era veterans: the Seabee Health Study. *Am J Epidemiol* 2002;**155**:1033–44.
- ⁴ Hernandez LM; Institute of Medicine (U.S.) and Committee on Measuring the Health of Gulf War Veterans. *Gulf War Veterans: Measuring Health.* Washington, DC: National Academy Press, 1999.
- ⁵ Kang HK, Mahan CM, Lee KY, Magee CA, Murphy FM. Illnesses among United States veterans of the Gulf War: a population-based survey of 30,000 veterans. *J Occup Environ Med* 2000;**42**:491–501.
- ⁶ Hoge CW, Auchterlonie JL, Milliken CS. Mental health problems, use of mental health services, and attrition from military service after returning from deployment to Iraq or Afghanistan. *JAMA* 2006;**295**:1023–32.
- ⁷ Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med* 2004;**351:**13–22.
- ⁸ Gray GC, Coate BD, Anderson CM *et al*. The postwar hospitalization experience of U.S. veterans of the Persian Gulf War. *N Engl J Med* 1996;**335**:1505–13.
- ⁹ Kulka RA, Schlenger WE, Fairbank JA et al. Trauma and the Vietnam War Generation: Report of Findings from the National Vietnam Veterans Readjustment Study. New York: Brunner/Mazel, 1990.

- ¹⁰ Unwin C, Blatchley N, Coker W *et al*. Health of UK servicemen who served in Persian Gulf War. *Lancet* 1999;**353**:169–78.
- ¹¹ Department of Veterans Affairs. Secretary Shinseki Announces New Efforts to Explore Health Consequences of Service in Vietnam. Washington DC: Department of Veterans Affairs, 2009.
- ¹² AFHS (Air Force Health Study). An Epidemiologic Investigation of Health Effects of Air Force Personnel Following Exposures to Herbicides: Study Protocol Initial Report. TX: USAF School of Aerospace Medicine, 1982.
- ¹³ Hotopf M, Hull L, Fear NT *et al*. The health of UK military personnel who deployed to the 2003 Iraq war: a cohort study. *Lancet* 2006;**367**:1731–41.
- ¹⁴ Secretary of Defense. Report to the Committee on National Security, House of Representatives, and the Armed Services Committee, US Senate, on Effectiveness of Medical Research Initiatives Regarding Gulf War Illnesses. Washington DC: Department of Defense, 1998.
- ¹⁵ Gray GC, Chesbrough KB, Ryan MA *et al.* The Millennium Cohort Study: a 21-year prospective cohort study of 140,000 military personnel. *Mil Med* 2002;**167**: 483–88.
- ¹⁶ Tate AR, Jones M, Hull L *et al.* How many mailouts? Could attempts to increase the response rate in the Iraq war cohort study be counterproductive? *BMC Med Res Methodol* 2007;**7**:51.
- ¹⁷ Fear NT, Jones M, Murphy D *et al*. What are the consequences of deployment to Iraq and Afghanistan on the mental health of the UK armed forces? A cohort study. *Lancet* 2010;**375**:1783–97.
- ¹⁸ Ryan MA, Smith TC, Smith B *et al.* Millennium Cohort: enrollment begins a 21-year contribution to understanding the impact of military service. *J Clin Epidemiol* 2007; **60**:181–91.
- ¹⁹ Smith B, Smith TC, Gray GC, Ryan MA. When epidemiology meets the Internet: Web-based surveys in the Millennium Cohort Study. *Am J Epidemiol* 2007;166: 1345–54.
- ²⁰ Smith TC; Millennium Cohort Study Team. The US Department of Defense Millennium Cohort Study: career span and beyond longitudinal follow up. *J Occup Environ Med* 2009;**51**:1193–201.
- ²¹ Dillman DA. Mail and Internet Surveys: The Tailored Design Method. 2nd edn. New York: Wiley, 2007.
- ²² Wells TS, Jacobson IG, Smith TC *et al.* Prior health care utilization as a potential determinant of enrollment in a 21-year prospective study, the Millennium Cohort Study. *Eur J Epidemiol* 2008;**23**:79–87.
- ²³ Smith TC, Smith B, Jacobson IG, Corbeil TE, Ryan MA. Millennium Cohort Study Team. Reliability of standard health assessment instruments in a large, populationbased cohort study. *Ann Epidemiol* 2007;**17**:525–32.
- ²⁴ LeardMann CA, Smith B, Smith TC, Wells TS, Ryan MA. Smallpox vaccination: comparison of self-reported and electronic vaccine records in the Millennium Cohort Study. *Hum Vaccin* 2007;**3**:245–51.
- ²⁵ Smith B, Wingard DL, Ryan MA, Macera CA, Patterson TL, Slymen DJ. U.S. military deployment during 2001–2006: comparison of subjective and objective data sources in a large prospective health study. *Ann Epidemiol* 2007;**17**:976–82.

- ²⁶ Smith B, Leard CA, Smith TC, Reed RJ, Ryan MA. Anthrax vaccination in the Millennium Cohort: validation and measures of health. *Am J Prev Med* 2007;**32**: 347–53.
- ²⁷ Smith TC, Jacobson IG, Smith B, Hooper TI, Ryan MA; for the Milliennium Cohort Team. The occupational role of women in military service: validation of occupation and prevalence of exposures in the Millennium Cohort Study. *Int J Environ Health Res* 2007;**17**:271–84.
- ²⁸ Goldberg D, Williams P. A User's Guide to the General Health Questionnaire. Windsor: NFER-Nelson, 1988.
- ²⁹ Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. *JAMA* 1999;**282**: 1737–44.
- ³⁰ Ware JE Jr. SF-36 health survey update. *Spine* 2000;**25**: 3130–39.
- ³¹ Iversen AC, van Staden L, Birtles C *et al.* The prevalence of common mental disorders and PTSD in the UK military: using data from a clinical interview-based study. *BMC Psychiatry* 2009;**9**:68.
- ³² Prins A, Ouimette P, Kimerling R *et al*. The Primary Care PTSD Screen (PC-PTSD): development and operating characteristics. *Prim Care Psychiatry* 2004;**9**:9–14.
- ³³ American Psychiatric Association. Electronic DSM-IV-TR plus. 1.0. Washington, DC: American Psychiatric Association, 2000.
- ³⁴ Babor T, Higgins-Biddle J, Saunders J, Monteiro M. AUDIT: The Alcohol Use Disorders Identification Test. 2nd edn. Geneva: World Health Organization, 2001.
- ³⁵ Ewing JA. Detecting alcoholism. The CAGE questionnaire. JAMA 1984;**252**:1905–07.
- ³⁶ Riddle JR, Smith TC, Smith B *et al.* Millennium Cohort: the 2001–2003 baseline prevalence of mental disorders in the U.S. military. *J Clin Epidemiol* 2007;**60**: 192–201.
- ³⁷ Smith TC, Ryan MA, Wingard DL, Slymen DJ, Sallis JF, Kritz-Silverstein D. New onset and persistent symptoms of post-traumatic stress disorder self reported after

deployment and combat exposures: prospective population based US military cohort study. *BMJ* 2008;**336**: 366–71.

- ³⁸ Richardson LK, Frueh BC, Acierno R. Prevalence estimates of combat-related post-traumatic stress disorder: critical review. Aust N Z J Psychiatry 2010;44:4–19.
- ³⁹ Sundin J, Fear NT, Iversen A, Rona RJ, Wessely S. PTSD after deployment to Iraq: conflicting rates, conflicting claims. *Psychol Med* 2009;**40**:367–82.
- ⁴⁰ Murphy D, Dandeker C, Horn O *et al*. UK armed forces responses to an informed consent policy for anthrax vaccination: a paradoxical effect? *Vaccine* 2006;**24:**3109–14.
- ⁴¹ Murphy D, Hull L, Horn O *et al*. Anthrax vaccination in a military population before the war in Iraq: side effects and informed choice. *Vaccine* 2007;**25**:7641–48.
- ⁴² Jacobson IG, Smith TC, Smith B, Wells TS, Reed RJ, Ryan MA. US military service members vaccinated against smallpox in 2003 and 2004 experience a slightly higher risk of hospitalization postvaccination. *Vaccine* 2008;**26**:4048–56.
- ⁴³ Wells TS, LeardMann CA, Smith TC *et al.* Self-reported adverse health events following smallpox vaccination in a large prospective study of US military service members. *Hum Vaccin* 2008;**4**:127–33.
- ⁴⁴ Allen JS, Skowera A, Rubin GJ, Wessely S, Peakman M. Long-lasting T cell responses to biological warfare vaccines in human vaccinees. *Clin Infect Dis* 2006;**43**:1–7.
- ⁴⁵ Granado N, Smith T, Swanson G *et al.* Newly-reported hypertension after military combat deployment in a large population-based study. *Hypertension* 2009;**54:**966.
- ⁴⁶ Smith B, Chu LK, Smith TC *et al.* Challenges of self-reported medical conditions and electronic medical records among members of a large military cohort. *BMC Med Res Methodol* 2008;**8:**37.
- ⁴⁷ Welch KE, LeardMann CA, Jacobson IG *et al.* Postcards encourage participant updates. *Epidemiology* 2009;**20**: 313–14.
- ⁴⁸ Iversen A, Liddell K, Fear N, Hotopf M, Wessely S. Consent, confidentiality, and the Data Protection Act. *BMJ* 2006;**332:**165–69.