Systematic reviews of psychological disorders, multisymptom illness and chronic fatigue syndrome in veterans deployed to the Gulf War, Afghanistan or Iraq War

Summary Report 2015
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1 Background

In the 1990-1991 Gulf War (Gulf War), a large multinational force was deployed to the Gulf area in response to the invasion of Kuwait by Iraq on 2 August 1990. In October 2001 in response to the September 11 attacks on the US, the United States of America (US) supported by the United Kingdom (UK), Australia, Canada, France and Germany and other nations began an invasion of Afghanistan (Operation Enduring Freedom, OEF). In March 2003, the Iraq War began (Operation Iraqi Freedom, OIF) when a combined force from the US, UK, Australia and Poland invaded Iraq. US forces withdrew from Iraq by December 2011.

The forces deployed by countries differed. For example, in contrast to US service members and UK personnel deployed during the Gulf War who were predominantly army land based forces, Australian personnel were primarily involved in sea and air surveillance (around 85% of deployed personnel were in the Royal Australian Navy) (1). In the Afghanistan and Iraq War, the Australian deployment involved the services of Air Force, Navy, Army, and Special Operations Task Group (2). The Army comprised the majority of deployed UK (3) and US active duty (4) personnel.

Although veterans of war deployment, including Gulf War, Afghanistan and Iraq War veterans have been found to be at increased risk of psychological disorders, posttraumatic stress disorder (PTSD) has tended to receive greater attention and publicity than other psychological disorders such as depression, alcohol use or other substance use disorders, or anxiety disorders such as generalised anxiety disorder (GAD).

Over the past 20 years there has been an increasing volume of literature published on veterans of the Gulf War, Afghanistan War and Iraq War, and systematic reviews can assist in synthesising what the literature is reporting across individual studies. The purpose of this project was to conduct systematic reviews and meta-analyses of studies that have compared psychological disorders, multisymptom illness and chronic fatigue syndrome (CFS) in veterans of deployments to the Gulf War, Afghanistan or the Iraq War, compared to military personnel who were not deployed to these conflicts.

2 Aims

The overall aim of this project was to conduct systematic reviews and meta-analyses of the literature to compare psychological disorders (depression, PTSD, GAD, alcohol use disorders, other substance use disorders (e.g., opioids, sedatives, hypnotics, anxiolytics, cocaine, cannabis) (herein termed substance use disorders for brevity), multisymptom illness and CFS in veterans of the Gulf War, Afghanistan and Iraq War compared with military comparison groups who were not
deployed to the corresponding conflicts. A further aim in the meta-analyses was to assess sources of variability, by subgroup analyses relevant to the particular meta-analysis being undertaken, to explore the factors most likely to result in study heterogeneity.

3 Methods

The searches, study selection and data extraction were conducted separately for psychological disorders, multisymptom illness and CFS; but as the methods were similar for the three broad outcome categories in Gulf War, Afghanistan and Iraq War veterans, the methods were described overall and the results were then presented separately for each of these three broad outcomes.

The health outcomes considered were:

- Psychological disorders of depression (major depression and dysthymia), PTSD, GAD, alcohol use disorders, substance use disorders (e.g., opioids, sedatives, hypnotics, anxiolytics, cocaine, cannabis), and (combined) any substance use disorder (i.e. alcohol and/or substance use disorders other than alcohol).
- Multisymptom illness, and
- CFS.

The definition used for inclusion of studies of multisymptom illness was based on an internationally accepted definition, specifically the Centers for Disease Control (CDC) definition (5, 6) developed by Fukuda et al. (5) and its variants. The CDC definition identifies multisymptom illness as present if the person has one or more chronic symptoms (for at least six months) from at least two of three categories: fatigue, mood-cognition (symptoms of feeling depressed, difficulty remembering or concentrating, feeling moody, feeling anxious, trouble finding the right words or difficulty sleeping) and musculoskeletal (symptoms of joint pain, joint stiffness or muscle pain), where the latter were the two categories identified in their factor analysis of symptoms reported in their study of US Gulf War veterans. For this systematic review, we used the CDC definition of multisymptom illness because it represented an internationally accepted definition of multisystem symptom reporting and was commonly available during the period of the review.

The definition used for inclusion of studies of CFS was based on an internationally accepted definition, specifically the 1994 international definition (7, 8) for defining CFS and other fatiguing illnesses.

Search criteria were developed and the international scientific literature was searched (1 January 1990 to 24 January 2014) in multiple electronic databases MEDLINE, MEDLINE In-Process, PsycINFO, Embase, Published International Literature on Traumatic Stress (PILOTS) and
Cochrane Reviews. In the multisymptom illness search, the System for Information on Grey Literature in Europe (SIGLE) was also included. Additional sources searched for non-peer review literature included the US, UK and Australian departments of veterans’ affairs and departments of defence websites. Studies were assessed for eligibility, according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations, quality and risk of bias (9). Overall risk of bias of the studies included in this systematic review was assessed using an instrument developed by Hoy et al. (10) which was used for the assessment of prevalence studies in the Global Burden of Disease Study 2010 (11). Individual items were assessed as high and low risk of bias, and used to assess overall risk of bias.

The search for papers which examined psychological health outcomes yielded 23,533 records, and 14,771 records remained after duplicates were removed. These records were screened to identify studies for full-text review by specified inclusion and exclusion criteria. After abstract review, 253 full-text articles were identified for further review and 49 of these were identified as eligible for inclusion in the review; 25 in Gulf War and 24 in Afghanistan/Iraq War veterans.

The search for papers which examined multisymptom illness yielded 2,573 records, with 2,445 records remaining after removal of duplicates. These records were screened to identify studies for full-text review by specified inclusion and exclusion criteria. After abstract review, 130 full-text articles were identified for further review, and seven eligible studies were identified reporting multisymptom illness according to the eligibility criteria.

The search for papers which examined CFS yielded 1,721 records, with 1,332 records remaining after duplicate removal. These records were screened to identify studies for full-text review by specified inclusion and exclusion criteria. After abstract review, 71 full-text articles were reviewed further, and 11 eligible articles were identified reporting CFS according to the eligibility criteria.

Quantitative and other relevant data for each individual study were extracted by standard data extraction forms developed for the review (descriptive data, summary measures of effect size, precision and assessment of risk of bias) and the findings of eligible studies were tabulated.

As heterogeneity (variability) of outcome was expected between studies, random effects meta-analyses (12, 13), for the outcomes under consideration were conducted to aggregate the odds ratios across the selected studies and produce pooled (or summary) odds ratios with 95% confidence intervals (OR, 95% CI).

Statistical heterogeneity was reported using the $I^2$ statistic which indicates variability in results across studies that is due to heterogeneity rather than chance, with larger values representing greater heterogeneity. Sources of variability were assessed by subgroup analyses relevant to the particular meta-analysis being undertaken to explore the factors most likely to result in study
heterogeneity. These included the outcome measure used (diagnostic interview; screening tool; self-reported physician diagnosis), type of multisymptom definition, adjusted vs unadjusted odds ratios, risk of bias (low, high), theatre of operation (Gulf War versus Afghanistan/Iraq War), and duty status (regular vs reservist) in Gulf War and Afghanistan/Iraq War veterans. Sensitivity analyses, excluding individual studies one at a time, were also conducted for all studies.

Publication bias was assessed by generated funnel plots and conducting the Egger test. A funnel plot is a graphical display of a measure of study precision plotted most commonly on the vertical axis, against effect estimate on the horizontal axis, that can be used to investigate whether there is a link between study size and effect estimate. All meta-analyses were performed using MetaXL.

4 Findings

The overall pattern of findings from these systematic reviews and meta-analyses of psychological disorders, multisymptom illness and CFS in Gulf War veterans, Afghanistan and Iraq War veterans was that for virtually all of the psychological disorders, the summary odds ratios (ORs) were elevated in Gulf War or Afghanistan/Iraq War veterans compared with military personnel who were not deployed to the corresponding conflict zone.

Depression in Gulf War veterans and Afghanistan/Iraq War veterans compared to non-deployed military personnel

Gulf War veterans had over twice the odds of experiencing depression (OR 2.28, 95% CI 1.88-2.76) and dysthymia or chronic dysphoria (OR 2.39, 95% CI 2.0-2.86) compared to non-deployed military personnel, based on a meta-analysis of 14 included studies. Heterogeneity for the summary odds ratio for depression was high ($I^2=75\%$). The elevated odds of depression were robust to sensitivity analysis excluding any individual study, to differences in overall risk of bias and psychological measures used. However, only five of the 14 studies investigated dysthymia or chronic dysphoria, and three of the five estimates were not statistically significant. In addition, two of the five studies were of chronic dysphoria, rather than the DSM-diagnosed condition of dysthymia.

The odds of depression in deployed Afghanistan/Iraq War veterans compared with non-deployed personnel (OR 1.58, 95% CI 1.14-2.17) were increased, based on a random-effects meta-analysis of ten studies. However, the heterogeneity across studies was very high ($I^2 = 98\%$) so the meta-analytic effect should be interpreted with caution in terms of the actual level of the increased odds. Subanalysis by type of outcome measure used to diagnose depression identified a statistically significant difference across the three reported diagnosis methods (namely International Classification of Diseases, 9th Revision (ICD-9) diagnosis, screening instrument, or other), with the
relationship suggesting that the more rigorous the outcome measure, the higher the odds ratio of depression in Afghanistan/Iraq War veterans. Other subgroup analyses did not identify a statistically significant difference between subgroups. Sensitivity analyses indicated that the overall OR did not change after excluding any individual study, the statistical significance did not change and heterogeneity remained high.

The P-value for the test for equality of the summary OR of depression in Gulf War veterans’ meta-analysis and the summary OR of depression in Afghanistan/Iraq War veterans’ meta-analysis was 0.055. This is suggestive of the odds of depression in Gulf War veterans being higher than in Afghanistan/Iraq War veterans compared with their non-deployed comparison groups respectively, but the difference between the two summary ORs narrowly missed statistical significance.

**PTSD in Gulf War veterans and Afghanistan/Iraq War veterans compared to non-deployed military personnel**

Based on a meta-analysis of 18 studies there was an increased odds of PTSD in Gulf War veterans compared with non-deployed personnel (OR 3.39, 95% CI 2.79-4.13). There was a moderate amount of statistical heterogeneity ($I^2 = 53\%$). In subanalysis, the summary odds ratio of PTSD in Gulf War veterans was increased in studies assessed as overall high risk of bias.

Based on a meta-analysis of 16 studies, there was an increased odds of PTSD in deployed Afghanistan/Iraq War veterans compared with non-deployed personnel (OR 2.12, 95% CI 1.65-2.72). However, there was a very high amount of statistical heterogeneity ($I^2 = 97\%$), so the meta-analytic effect should be interpreted with caution in terms of the actual level of the increased odds. Subanalyses and sensitivity analyses did not provide an explanation for the high heterogeneity.

The P-value for the test for equality of the summary OR of PTSD in Gulf War veterans and summary OR of PTSD in Afghanistan/Iraq War veterans was 0.004, suggesting that the summary OR of PTSD was statistically significantly higher in Gulf War than in Afghanistan/Iraq War veterans.

**Alcohol use, substance use, and (combined) any substance use disorders (i.e. alcohol and/or substance use disorders) in Gulf War veterans and Afghanistan/Iraq War veterans compared to non-deployed military personnel**

In relation to alcohol use disorders and substance use disorders (e.g., opioids, sedatives, hypnotics, anxiolytics, cocaine, cannabis), and (combined) any substance use disorder (i.e. alcohol and/or substance use disorders); nine studies were included in the meta-analyses in Gulf War veterans, and nine studies reported on alcohol or substance use disorders in Afghanistan/Iraq War veterans and seven discrete studies were included in the meta-analyses. Pooled analyses based on a random-effects model yielded a summary OR 1.33 (95% CI 1.22-1.46) for alcohol (n=7
studies), OR 2.13 (95% CI 0.96-4.72) for substance use disorders (n=3 studies), and OR 1.35 (95% CI 1.25-1.46) for any substance use disorders (n=9 studies) in Gulf War veterans; and OR 1.36 (95% CI 1.11-1.66) for alcohol (n=7 studies) and OR 1.14 (95% CI 1.04-1.25) for substance use disorders (n=4 studies) in Afghanistan/Iraq War veterans. One study that reported any substance use as an outcome in Afghanistan/Iraq War veterans was reported separately.

There were no statistically significant associations between theatre of war and alcohol use disorders or substance use disorders.

GAD in Gulf War veterans and Afghanistan/Iraq War veterans compared to non-deployed military personnel

Based on a random-effects meta-analysis of five included studies of GAD, Gulf War veterans had increased odds of GAD compared with non-deployed personnel (OR 3.04, 95% CI 1.95-4.75). There was a low to moderate amount of statistical heterogeneity ($I^2 = 35\%$). Stratification by case definition the diagnostic interview subgroup and screening tool subgroup had broadly similar ORs. In sensitivity analysis, excluding the reservists’ subgroup study resulted in the most change in the summary OR, a decrease to 2.40 (95% CI 1.65-3.49).

Based on a random-effects meta-analysis of three included studies, the summary OR of GAD in Afghanistan/Iraq War compared with non-deployed personnel was 1.20 (95% CI 1.00-1.44). Heterogeneity was not at a detectable level. Further subanalyses could not be undertaken due to the small number of studies. However, in a sensitivity analysis when a study that was undertaken solely on reservists and National Guard was excluded, the OR decreased and was not significant. The summary OR of GAD in Gulf War veterans was statistically significantly higher than the summary OR for Afghanistan/Iraq War veterans.

Multisymptom illness in Gulf War veterans compared to non-deployed military personnel

Seven eligible studies were identified reporting multisymptom illness according to the eligibility criteria which included studies that used the CDC definition for multisymptom illness. All of these studies were in Gulf War veteran populations and no eligible studies were identified in Afghanistan or Iraq War veteran populations. Meta-analysis of the seven eligible studies showed that the odds of multisymptom illness were more than two and a half times greater in Gulf War veterans compared with non-deployed comparison groups (OR 2.74, 95% CI 2.01-3.72). There was a high amount of statistical heterogeneity ($I^2=92\%$). Subanalysis conducted based on five studies that used the CDC definition, using three groupings of symptoms to define a multisymptom illness case, showed that the OR increased slightly to around three fold in Gulf War veterans compared with non-deployed military comparison group and heterogeneity decreased slightly ($I^2=76\%$).
CFS in Gulf War veterans compared to non-deployed military personnel

Based on a random-effects meta-analysis of the seven studies that met the eligibility criteria and were included in the meta-analysis of CFS in Gulf War veterans, there was an increased odds of CFS in Gulf War veterans compared with non-deployed personnel (OR 7.62, 95% CI 3.91-14.85). There was a moderate amount of statistical heterogeneity (I² = 52%). There were no eligible studies identified in Afghanistan or Iraq War veteran populations.

Table 1 summarises the main meta-analysis summary ORs for psychological disorders, multisymptom illness and CFS, and the assessment of difference between the summary ORs in Gulf War veterans and in Afghanistan/Iraq War veterans where applicable.

Table 1 Main meta-analysis summary odds ratios for psychological disorders, multisymptom illness and chronic fatigue syndrome (CFS) in Gulf War, Afghanistan/Iraq War veterans compared with non-deployed personnel

<table>
<thead>
<tr>
<th>Main health outcome</th>
<th>Gulf War veterans</th>
<th>Afghanistan/Iraq War veterans</th>
<th>P-value for the test for equality of the summary OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I²=75%</td>
<td>I²=98%</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>2.28 (1.88-2.76)</td>
<td>1.58 (1.14-2.17)</td>
<td>0.055</td>
</tr>
<tr>
<td>Dysthymia or chronic dysphoria</td>
<td>2.39 (2.0-2.86)</td>
<td>n.a.</td>
<td></td>
</tr>
<tr>
<td>PTSD</td>
<td>3.39 (2.79-4.13)</td>
<td>2.12 (1.65-2.72)</td>
<td>0.004</td>
</tr>
<tr>
<td>Alcohol use disorders</td>
<td>1.33 (1.22-1.46)</td>
<td>1.36 (1.11-1.66)</td>
<td>0.862</td>
</tr>
<tr>
<td>Substance use disorders</td>
<td>2.13 (0.96-4.72)</td>
<td>1.14 (1.04-1.25)</td>
<td>0.053</td>
</tr>
<tr>
<td>Any substance use disorder</td>
<td>1.35 (1.25-1.46)</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Generalised anxiety disorder</td>
<td>3.04 (1.95-4.75)</td>
<td>1.20 (1.00-1.44)</td>
<td>Respective 95% CI did not overlap</td>
</tr>
<tr>
<td>Multisymptom illness</td>
<td>2.74 (2.15-3.51)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFS</td>
<td>7.62 (3.91-14.85)</td>
<td>I² = 52%</td>
<td></td>
</tr>
</tbody>
</table>

n.a. Not applicable.
* 'Any substance use' outcome was measured in Afghanistan/Iraq War veterans' study (14) and was reported separately.
† There were no studies identified of multisymptom illness or CFS in Afghanistan/Iraq War veterans.

5 Discussion

These systematic reviews and meta-analyses, based on international literature published between January 1990 and January 2014, of psychological disorders, multisymptom illness and CFS in Gulf War veterans, Afghanistan and Iraq War veterans found that for virtually all of the psychological disorders, the summary ORs were elevated in Gulf War or Afghanistan/Iraq War veterans.
compared with military personnel who were not deployed to the corresponding conflict zone. The summary ORs for PTSD and GAD in Gulf War veterans compared with non-deployed personnel were statistically significantly higher than the summary ORs of PTSD and GAD in Afghanistan/Iraq War veterans respectively. The summary odds of depression were higher in Gulf War veterans than in Afghanistan/Iraq War veterans and this narrowly missed statistical significance. Any substance use disorders (i.e. alcohol and/or other substance use disorders) were elevated in Gulf War veterans compared with non-deployed personnel, and substance use disorders were elevated in Afghanistan/Iraq War veterans compared with non-deployed military personnel. However, substance use disorders were relatively under researched, with a small number of studies having been identified through the systematic review. The meta-analytical ORs of multisymptom illness and of CFS in Gulf War veterans compared with non-deployed personnel were elevated. There were no studies identified through the search strategy for the systematic review of multisymptom illness and of CFS in Afghanistan and Iraq War veterans.

The mental health in reservists compared with active duty/regular veteran personnel post deployment has been of concern in relation to the increased proportion of US or UK National Guard or reservist forces deployed to Afghanistan/Iraq (15-18), and although the relationship between active or reservist status on psychological health post deployment was not a primary research question in this project, regular versus reservist status was a subgroup analysis undertaken for a limited number of psychological outcomes. There were no important differences identified in the likelihood of PTSD in reservists compared with regular personnel deployed to the Gulf War or to Afghanistan/Iraq War. The summary estimate of the likelihood of alcohol use disorders was slightly higher, but not statistically significant, in reservists compared with regular personnel deployed to Afghanistan/Iraq War.

**Strengths and limitations**

Our series of systematic review and meta-analyses had several strengths including a comprehensive search strategy with studies identified through a search using multiple electronic databases from 1990 to 2014; also review and data extraction were conducted according to established criteria. We addressed methodological limitations of previous reviews in this field, updated the literature with more recently published studies, and assessed overall risk of bias in individual studies that were included in the systematic reviews and meta-analyses, which had not been done in previous reviews (19-22) of a similar nature, and the robustness of the results to risk of bias through subanalysis. However, many of these previous reviews discussed essential biases of included studies individually, and a narrative description of the studies, but this is not as strong as a formal assessment of risk of bias.
Our rigorous methodology of only including studies with a military non-deployed comparison group eliminated many methodological concerns of previous reviews in the field by concentrating on the psychological outcome or multisymptom illness or CFS as the condition of interest, and which may have included papers which used civilian comparison groups. We excluded treatment seeking self-selected populations that are more likely to experience higher rates of disorders and may not be representative of the overall military population that were deployed. We also excluded several well conducted prevalence studies that did not have any military comparison group, since comparing prevalence studies using different methodologies makes it very difficult to ascertain whether the differences in associations were due to difference in deployment or different methodologies used in the studies rather than comparison with similar but non-deployed military personnel (9).

A limitation was the small number of studies identified in some reviews, such as GAD and reported substance use disorders in Gulf War and Afghanistan/Iraq War veterans, which limited the statistical power in some meta-analyses that involved a small number of studies and also limited the capacity to undertake further subgroup analyses for some outcomes. No studies were identified for the outcomes of multisymptom illness and chronic fatigue syndrome over the period of our literature search. However, given our extensive search methodology, we consider it unlikely that we missed relevant literature. Where results were reported separately in the studies for veterans deployed to the Iraq War only or to Afghanistan only compared with non-deployed personnel these were reported, but the great majority of included studies grouped these veterans in reported findings, and subanalyses could not be undertaken by theatre of deployment.

Although PTSD has often received more attention and publicity in relation to military and veterans’ health, we are not aware of any previous systematic reviews that have estimated comprehensively the risk of depression, alcohol use disorders, substance use disorders, and GAD in Gulf War and Afghanistan/Iraq War veterans. Our systematic reviews have extended and updated previous reviews undertaken for multisymptom illness and chronic fatigue and symptom based conditions and have also undertaken meta-analyses for the first time.

Multisymptom illness and CFS have been identified contextually more with the Gulf War than with deployments to Afghanistan and the Iraq War. However, to the knowledge of the authors of this report, a comprehensive systematic review of the literature on these symptom based conditions in veterans of other deployments to this area of operations, has not been undertaken. The eligibility criteria in our systematic review for inclusion of studies regarding multisymptom illness and CFS included internationally accepted case definitions for the epidemiological study of these conditions (5-8). The US IOM 2014 report on development of a consensus definition on chronic multisymptom illness (23) was published towards the end of the research process, but the IOM
Committee recommended that the US Veterans Affairs (VA) consider the use of the CDC definition (and Kansas definition (24)) of multisymptom illness because they capture the most commonly reported symptoms by Gulf War veterans.

Gulf War veteran health studies used a variety of definitions to investigate fatigue related outcomes in veterans including chronic fatigue caseness based on the Chalder Fatigue Scale (25), however we used the more rigorous 1994 international definition (7, 8) for defining CFS as the outcome measure for inclusion. It is possible that studies of Afghanistan and Iraq War veterans have assessed fatigue in veterans based on less rigorous definitions than CFS, including screening instruments and scales, but these were not considered in this systematic review. There are also various other approaches to defining multisymptom illnesses in Gulf War veterans, including defining Gulf War illnesses, that were not included in our review, based on our eligibility criteria.

The focus of each of the systematic reviews was the outcome under consideration, eg depression or PTSD or alcohol use disorder. We recognise that many Gulf War veterans and comparison group subjects with depression, for example, may also meet criteria for other psychological disorders including PTSD, substance use disorders, and anxiety disorders (1, 26). A detailed examination of this comorbidity between psychological disorders, however, was beyond the scope of this review and would detract from the primary focus.

Our systematic reviews and meta-analyses included studies across veteran cohorts from the US, UK, Australia, Germany and Canada, the majority of which sampled across all three services. The deployed forces of the countries from which the veteran cohorts were selected varied, including by whether the forces deployed to the Gulf War or to the Afghanistan/Iraq War. These variations included different type of forces contributed, e.g. relative contributions of Army, Navy and Air-Force or National Guard or reservist forces, and variations in the demographic composition of personnel in the deployed forces including the proportion of deployed female personnel. The included studies all included a non-deployed comparison group, which was the focus of our overall aim and comparison, and the majority adjusted for possible demographic and military service confounding factors. The meta-analyses for health outcomes under consideration did not did not undertake subgroup analyses by branch of service (other than regular vs reservist) or by gender of deployed personnel. Multiple factors influence health outcomes including cultural differences, different veteran health care and general health care systems in different countries. The main aim in these systematic reviews was to consider the summary ORs comparing the health outcome of interest in deployed compared with non-deployed personnel combining the ORs from the eligible studies.

Undertaking these systematic reviews has assisted in drawing conclusions about consistency of the results of studies in relation to psychological outcomes in Gulf War veterans, Afghanistan and Iraq War veterans, and multisymptom illness and CFS in Gulf War veterans compared to personnel
who were not deployed to a war zone or who were deployed elsewhere. Conducting meta-
analyses and presenting the outputs produced visual and comparable summary effect estimates of 
these outcomes in Gulf War veterans, Afghanistan and Iraq War veterans compared with non-
deployed military personnel and quantified this in overall summary measures. By reporting 
summary estimates, it is easier and quicker for readers of this report, including health policy 
makers and service providers, non-researcher veterans, and clinicians to gain an overview of the 
relevant literature.

6 Implications for policy and programs

An important finding from the current systematic reviews and meta-analyses was that virtually all of 
the psychological disorders under study of depression, PTSD, alcohol use disorder and substance 
use disorders, and GAD were elevated in troops deployed to the Middle East area of conflicts over 
the past 20 years compared with non-deployed military personnel. Although much attention and 
general awareness has focused on PTSD and the increased risk of PTSD associated with 
deployment to war and conflict zones, substantially less has focused on depression and other 
psychological disorders. These systematic reviews and meta-analyses show that these 
psychological conditions are also elevated in Gulf War and Afghanistan/Iraq War deployed 
compared with non-deployed personnel and poorer psychological health is not restricted to PTSD.

A further important finding is that the odds of multisymptom illness and CFS were significantly 
elevated in Gulf War veterans compared with non-deployed military personnel. Studies meeting 
the inclusion criteria for the systematic review of multisymptom illness and of CFS were identified 
in Gulf War veteran study populations, but not in Afghanistan or Iraq War veteran study 
populations. This could suggest that these conditions were not a primary concern or complaint in 
the context of Afghanistan/Iraq War veterans’ health. It is somewhat surprising that studies of 
Afghanistan/Iraq War veterans did not include a case definition of multisymptom illness or CFS 
similar to that employed in studies of previous veterans to that conflict zone; however they may 
have employed alternative or less rigorous definitions that did not meet our inclusion criteria.

In considering the implications of our findings, in Gulf War veterans there is a wide range of both 
physical and psychological conditions that are also increased compared with non-deployed 
personnel. In Afghanistan/Iraq War veterans compared with non-deployed personnel depression, 
alcohol use disorders, substance use disorders, GAD, and PTSD, are also increased. These 
findings serve as a reminder of the importance of considering these psychological conditions in 
assessing and managing veterans’ health and the importance of assessing the physical health of 
veterans in clinical practice and in veteran health research studies.
The most likely reason for the finding of increased alcohol use disorders and substance use disorders is that alcohol and other drugs are being used to “self-medicate” – to ameliorate other psychological or physical problems (27). This seems a plausible explanation given the high rates of depression and other psychological conditions in troops deployed to the Gulf War (19) and to the Afghanistan/Iraq War (28). Although the small numbers of studies of substance use disorders in Gulf War veterans limited power to detect a statistical difference between the study groups, stigma around illicit substances may have resulted in some underreporting of other substance abuse. The military handles alcohol and tobacco, legal substances, very differently to illicit substances.

Based on random-effects meta-analysis in the eligible studies, there was an increased odds of depression and of PTSD in deployed Afghanistan/Iraq War veterans compared with non-deployed personnel. However, there was a very high amount of statistical heterogeneity in each of the main analyses, so the actual size of the increased meta-analytic effect should be interpreted with caution. No explanation, investigated through subanalyses, was found for this high heterogeneity. Possible explanations for consideration are that Gulf War veterans who are now older have more chronic conditions, which have stabilised, whereas psychological conditions in younger veterans of more recent conflicts fluctuate more. It is well established that there is a dose response relationship between combat exposure and PTSD, an underlying factor in the heterogeneity observed in the meta-analysis of the association between PTSD and Afghanistan/Iraq War deployment compared with that in the meta-analysis of PTSD and Gulf War deployment may be a greater variation in the types of experiences veterans had in the more recent conflicts in the Middle East. Other Afghanistan/Iraq War deployment related factors such as the possibility of multiple deployments, variables within deployments, the chronicity of the overall deployment period, and the potential for other deployments at a time of increased operational tempo may also have contributed to this observed heterogeneity.

The odds of psychological disorders were all slightly greater in Gulf War veterans and the summary ORs for PTSD and GAD were statistically significantly higher than in Afghanistan/Iraq War veterans, and may reflect a level of chronicity. Psychological disorders tend to increase post deployment; the rate of onset of symptomatology of each broad DSM-IV diagnostic category was found to peak in the first two years following the Gulf War, in Australian Gulf War veterans, and then subsided. This pattern was particularly noticeable in the case of alcohol disorders (26).

The presentation of idiopathic physical symptoms including multisymptom illness and fatigue related conditions including symptoms of fatigue and chronic fatigue are likely to be to the person’s general medical practitioner. The presentation of these symptoms and conditions are not as likely to be through the mental health system. With overall increased odds of multisymptom illness and of CFS in Gulf War veterans, departments of veterans’ affairs (Australian and overseas) need to
work with general practitioners and primary care providers in relation to this symptomatology and symptom burden and conditions.

Our findings have important policy and program implications. About 697,000 US troops were deployed to the Gulf War, with other coalition forces (from countries such as the UK, France, Canada and Australia) amounting to nearly 260,000 at their peak personnel strength (29). Over two million US veterans have deployed to the Afghanistan and Iraq conflicts (30) in a coalition of 49 countries with the UK providing the second largest force. Increased risk of any condition in veteran populations of these sizes is clearly a concern.

While disorders such as PTSD and depression have been the primary focus, it is also important that the elevated risk of substance use disorders in veterans is recognised, as there is a strong association between those disorders and substance use disorders (31, 32). Furthermore, individuals with PTSD and depression co-occurring with substance use disorders often have worse treatment outcomes (33). Substance (and alcohol) use disorders are particularly troubling because of the powerful impact on behaviour, on the individual's health as well as impacts on family, community and society as a whole, in addition to the difficulties in diagnosis and management of comorbid disorders (34).

Further, there are circumstances and exposures associated with the Afghanistan and Iraq War deployments which may render a systematic review of the literature thus far highly pertinent. For example, the level of traumatic brain injury from these deployments has been associated with increased psychiatric illness outcomes (35). An examination of the relationship between traumatic brain injury and psychological disorders was not in the scope of this review.

An investigation by Hoge (28) reported that combat duty in Iraq was associated with high utilisation of mental health services and attrition from military service after deployment, and that the high rate of mental health services utilisation post-deployment is a challenge for resource allocation. In the context of our reviews which have found the summary ORs for the odds of all psychological disorders to be elevated in Afghanistan/Iraq War veterans and virtually all in Gulf War veterans, this finding have important implications for health service policy and delivery.

Change in the demographic structure of deployed forces, e.g. the proportion of reservists deployed to war zones may affect the physical or psychological health risk of the veteran population relative to their non-deployed counterparts. Individual studies may investigate these risk factors in relation to health outcomes in single study populations, but systematic reviews, which synthesise literature reported across individual studies in veteran populations from different countries, can provide a reliable estimate of risk factors that clinicians and policymakers need to be aware of when managing veterans’ health.
7 Implications for future research

Our systematic review showed that substance use disorders were generally under researched. For example, further studies with increased power are needed to assess substance use disorder risk in Gulf War veteran populations, and this is a consideration for future research studies.

Our systematic reviews considered psychological health outcomes, multisymptom illness and CFS and considered possible explanations for heterogeneity across studies. The methodology could be extended to assess the effect of important risk factors for these health outcomes, including military service exposures, different types of forces deployed e.g. branch of service, and vulnerable populations e.g. gender differences in deployed personnel. The differences that were observed in the summary ORs in health outcomes between Gulf War veterans and Afghanistan/Iraq War veterans could be compared again in the future, repeating the search and systematic review to update the studies and the meta-analyses, to investigate whether the differences change over time.

Influences on health outcomes are multifactorial but the influence of cultural factors and veteran and general population health care systems and services and uptake of those services for the health outcomes of interest could provide a useful comparison between countries that have deployed forces to the same conflicts, identify potential gaps, and service as an evidence base for future interventions.

8 Conclusions

Our systematic reviews and meta-analyses found that nearly all of the psychological disorders under study, i.e. depression, PTSD, GAD, alcohol use disorders, and substance use disorders were elevated in troops deployed to the Middle East area of conflicts over the past 20 years compared with non-deployed military personnel. Any substance use disorders (i.e. alcohol and/or other substance use disorders) were elevated in Gulf War veterans compared with non-deployed personnel, and substance use disorders were elevated in Afghanistan/Iraq War veterans compared with non-deployed military personnel, but further studies with increased statistical power are needed to assess the association with substance use disorders in Gulf War veterans.

Furthermore, the summary odds of PTSD and GAD were statistically significantly higher in Gulf War veterans compared with the summary odds in Afghanistan/Iraq War veterans. The summary odds of depression were higher in Gulf War veterans than the summary odds of depression in Afghanistan/Iraq War veterans and this narrowly missed statistical significance. There was a high level of heterogeneity observed between studies of Afghanistan/Iraq War veterans, PTSD, depression and alcohol use disorders in particular, that was not accounted for in subgroup
analyses. A possible explanation of this heterogeneity could be a more fluctuating pattern of psychological disorders in younger veterans of more recent conflicts in Afghanistan/Iraq Wars and/or more variability in exposures/experiences during deployment to these conflicts as distinct to chronicity or stability of psychological disorders in Gulf War veterans. However, there were too few studies to be able to examine temporal relationships.

A further important finding is that the odds of multisymptom illness and CFS were significantly elevated in Gulf War veterans compared with non-deployed military personnel. Studies meeting our eligibility criteria were not identified in Afghanistan/Iraq War veterans. Idiopathic symptoms contributing to multisymptom illness and CFS are more likely to present to general practitioners than through the mental health system and Veterans’ Affairs departments could work with general and primary care providers to address this burden of symptom reporting.

The main aim of these systematic reviews and meta-analyses was to consider the summary ORs comparing the health outcome of interest in deployed compared with non-deployed personnel combining the ORs from the eligible studies. However, the methodology could be extended to assess the effect of important risk factors for these health outcomes, including different types of forces deployed e.g. branch of service, military service exposures, and vulnerable populations e.g. gender differences. This body of research has highlighted some key areas that warrant consideration for policy makers and future researchers including cultural differences, the length of time since the war and deployment and the impact on health, the influence of veteran and general population health care systems between countries that are some of the factors that influence health outcomes and could be compared as a basis for future policy development and intervention.

9 References


