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Complete List of Authors:	Forbes, David; University of Melbourne, Psychiatry Pedlar, David; Canadian Institute for Military and Veteran Health Research Adler, Amy; Center for Military Psychiatry and Neuroscience Research; Walter Reed Army Institute of Research Bennett, Clare; New Zealand Defence Force Bryant, Richard; University of New South Wales Busuttil, Walter; Combat Stress Cooper, John; University of Melbourne, Psychiatry Creamer, Mark; University of Melbourne, Psychiatry Fear, Nicola; King's College London, ACDMH Greenberg, Neil; King's College London Heber, Alexandra; Veterans Affairs Canada Hinton, Mark; University of Melbourne, Psychiatry Hopwood, Mal; University of Melbourne, Psychiatry Jetly, Rakesh; Canadian Armed Forces Lawrence-Wood, Ellie; University of Adelaide McFarlane, Alexander; University of Melbourne, Psychiatry; University of Adelaide Metcalf, Olivia; University of Melbourne, Psychiatry O'Donnell, Meaghan; University of Melbourne, Psychiatry Phelps, Andrea; University of Melbourne, Psychiatry Richardson, J. Don; Western University, Psychiatry; McDonald/Franklin OSI Research Centre

	Sadler, Nicole; University of Melbourne, Psychiatry Schnurr, Paula; National Center for Post Traumatic Stress Disorder; Dartmouth College Geisel School of Medicine, Psychiatry Sharp, Marie-Louise; King's College London, King's Centre for Military Health Research Thompson, James; Veterans Affairs Canada Ursano, Robert; Uniformed Services University of the Health Sciences F Edward Hebert School of Medicine Van Hooff, Miranda; University of Adelaide Wade, Darryl; University of Melbourne, Psychiatry Wessely, Simon; King's College London, ACDMH
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Treatment of military-related posttraumatic stress disorder: Challenges, innovations, and the way forward

David Forbes[a]*, David Pedlar[b]*, Amy B. Adler[c]**, Clare Bennett[d], Richard Bryant[a,e], Walter Busuttil[f], John Cooper[a], Mark C. Creamer[a], Nicola T. Fear[g,h], Neil Greenberg[g], Alexandra Heber[i,] Mark Hinton[a], Mal Hopwood[a], Rakesh Jetly[j], Ellie Lawrence-Wood[k], Alexander McFarlane[a,k], Olivia Metcalf[a], Meaghan O'Donnell[a], Andrea Phelps[a], J. Don Richardson[l,m], Nicole Sadler[a], Paula P. Schnurr[n], Marie-Louise Sharp[g], James M. Thompson[i], Robert J. Ursano[o], Miranda Van Hooff[k], Darryl Wade[a], and Simon Wessely[g]

[a] *Centenary of Anzac Centre, Phoenix Australia- Centre for Posttraumatic Mental Health, Department of Psychiatry, University of Melbourne, Carlton, Australia;*

[b]*Canadian Institute for Military and Centre for Posttraumatic Mental Health Veteran Health Research, Canada*

[c]*Center for Military Psychiatry and Neuroscience, Walter Reed Army Institute of Research, Silver Spring, Maryland, U.S*

[d]*New Zealand Defence Force, New Zealand*

[e]*School of Psychology, University of New South Wales, Sydney, Australia*

[f]*Combat Stress, United Kingdom*

[g]*King's Centre for Military Health Research, King's College London, London, United Kingdom*

[h]*Academic Centre for Military Mental Health Research, London, United Kingdom*

[i]*Veterans Affairs Canada, Charlottetown, Canada*

[j]*Directorate of Mental Health, Canadian Armed Forces, Ottawa, Canada*

[k]*Centre for Traumatic Stress Studies, University of Adelaide, Adelaide, Australia*

[l]*Department of Psychiatry, Western University, London, Canada*

[m]*McDonald/Franklin OSI Research Centre, London, Canada*

[n]*National Center for PTSD, White River Junction, VT, USA, and Department of Psychiatry, Geisel School of Medicine, Hanover, NH, USA*

[o]*Center for the Study of Traumatic Stress, Department of Psychiatry, Uniformed Services University School of Medicine, Bethesda, Maryland, USA*

[p]*Department of Psychiatry, University of Ottawa, Canada*

** Denotes joint first authors*

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Please address correspondence concerning this article to:
Professor David Forbes
Level 3, Alan Gilbert Building, 161 Barry St
Carlton AUSTRALIA 3053
dforbes@unimelb.edu.au
Phone: +61 03 9035 5599
Fax: +61 03 9035 7526

Abstract

Posttraumatic stress disorder (PTSD) is one of the common mental disorders in military and veteran populations. Considerable research and clinical opinion has been focused on understanding the relationship between PTSD and military service and the implications for prevention, treatment, and management. This paper examines factors associated with the development of PTSD in this population, considers issues relating to engagement in treatment, and discusses the empirical support for best practice evidence-based treatment. The paper goes on to explore the challenges in those areas, with particular reference to treatment engagement and barriers to care, as well as treatment non-response. The final section addresses innovative solutions to these challenges through improvements in agreed terminology and definitions, strategies to increase engagement, early identification approaches, understanding predictors of treatment outcome, and innovations in treatment. Treatment innovations include enhancing existing treatments, emerging non trauma-focused interventions, novel pharmacotherapy, personalised medicine approaches, advancing functional outcomes, family intervention and support, and attention to physical health.

Posttraumatic stress disorder in veteran and military populations

Posttraumatic stress disorder (PTSD) is one of the common mental disorders in military and veteran populations (Magruder & Yeager, 2009; Williamson, Stevelink, Greenberg, & Greenberg, 2018; Wisco et al., 2014). (The term "veteran" has several meanings in different contexts. Sometimes, for example, it refers to anyone who has left the military, regardless of their combat experiences and deployment history, while at other times it refers to anyone who has completed an operational deployment, regardless of whether he/she is still serving. We recognise that this causes confusion in the research literature and have tried, where relevant, to differentiate the two). While the disorder can present in mild forms, PTSD can often become a chronic disorder resulting in substantial functional impairment and reduced quality of life (Australian Centre for Posttraumatic Mental Health, 2013; Bruffaerts et al., 2012; Schnurr, Lunney, Bovin, & Marx, 2009). The Diagnostic and Statistical Manual of Mental Disorder 5th Edition (DSM-5) describes PTSD as having four symptom clusters: (1) re-experiencing the traumatic event, including recurring intrusive memories, flashbacks, or dreams of the trauma; (2) intentional avoidance of traumatic memory triggers; (3) changes in mood and/or thoughts, such as feelings of anxiety, sadness, shame or anger, negative thoughts about the self or others, or emotional numbing; and (4) hyperarousal in the form of irritability, hypervigilance, and trouble with concentration and sleep (American Psychiatric Association, 2013). The ICD-11 PTSD criteria are somewhat simpler and focus on the three symptom clusters of re-experiencing, active avoidance, and hyperarousal (Maercker et al., 2013). The DSM-5 also introduced a dissociative subtype characterised by high levels of either depersonalisation or derealisation.

PTSD is not unique to military and veteran populations. Veteran populations, however, are characterised by several factors that may influence the development and

nature of the disorder. In addition to the risk of exposure to the trauma of war, for example, adverse childhood experiences prior to joining the military (a risk factor for the development of later mental health problems) are reported at increased rates among those who have served in the military (Blosnich, Dichter, Cerulli, Batten, & Bossarte, 2014). Transition to and from military life creates many adjustment challenges, potentially disrupting identity and increasing risk for development of mental health problems. Military populations report higher rates of musculoskeletal conditions and chronic pain than civilian controls, and chronic physical disorders have been shown to precede depression and anxiety in many cases (Andersen, Wade, Possemato, & Ouimette, 2010; Thompson et al., 2016). This combination of mental and physical health conditions has a synergistic effect on functional impairment (especially in military roles) which, in turn, may significantly contribute to worsening of mental health problems in veterans (Thompson et al., 2015).

Taken together, those factors represent a unique risk profile for the development of mental health problems among military and veteran populations. Once problems develop, cultural factors may affect the person's willingness to acknowledge mental health issues, as well as how those problems are expressed (Sharp et al., 2015), highlighting the need for specialised understanding among practitioners about military service and the need to build trust with veterans in clinical settings. Those factors, of course, may also adversely affect engagement in, and response to, treatment. Without effective engagement, individuals with PTSD (whether military or civilian) are at risk of a chronic course and long duration of illness with significant negative consequences for themselves and their families. Regrettably, a detailed discussion of the impact on families is beyond the scope of this paper. Suffice to say at this point, however, that it is

of the utmost importance to actively support families – both in their own right and as part of PTSD recovery for the service member (Fear et al., 2018).

Trauma exposure and prevalence of PTSD in military and veteran populations

Military-related PTSD can be the result of a diverse range of operational experiences including combat, peacekeeping and humanitarian deployments, as well as non-deployment trauma. Traumatic exposures may include direct threat to the self or others, or witnessing significant human suffering and being prevented through rules of engagement from intervening to protect non-combatants. Many of these scenarios are characterised by moral ambiguity and complexity. There is increasing recognition of moral injury – the psychological, social and spiritual impacts of exposure to traumatic events that transgress deeply held moral beliefs (Litz et al., 2009) or involve betrayal of "what's right" (Shay, 2014). These exposures can occur repeatedly against a background of long periods spent in demanding operational contexts, high levels of threat, and hostile physical environments.

Military personnel operating in a combat role have an increased likelihood of developing PTSD (Prigerson, Maciejewski, & Rosenheck, 2001). However, not all military trauma is deployment related. Non-deployment stressors are part of everyday military life, including realistic training exercises conducted under extreme conditions, often with dangerous machinery and live ammunition, in order to prepare them for their roles in operational environments. Military sexual trauma (MST), which affects both men and women (although proportionately more women), is associated with increased risk of PTSD as well as other comorbidities (Kimerling et al., 2010; Wilson, 2018). Inevitably, as a military career progresses, there is increased likelihood of experiencing multiple potentially traumatic events, putting individuals at greater risk of the effects of

cumulative trauma exposures. A more sophisticated understanding of trauma exposures in military experiences beyond the warzone has been influential in informing treatment approaches to military-related PTSD.

Estimates of PTSD prevalence in veteran populations vary widely depending, for example, on the era, the percentage of those who deployed, and the specific nature of the deployment. For the veteran population as a whole (i.e., across cohorts and including both deployed and non-deployed), the best estimates are usually around 8% lifetime and 5% current PTSD (Wisco et al., 2014). These prevalence rates are comparable to, or slightly higher than, those for civilian populations (Chapman et al., 2012; Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012; Woodhead et al., 2011). Specific deployments, however, can be associated with substantially higher rates, with estimates of lifetime PTSD prevalence varying up to 35% (O'Toole, Catts, Outram, Pierse, & Cockburn, 2009; Xue et al., 2015). Experiences on deployment, such as increased combat exposure, fear of being killed or seriously injured, discharging a weapon, and witnessing someone being wounded or killed, substantially increase the risk for PTSD (Xue et al., 2015). PTSD prevalence in military and veteran populations also varies across nations, a function of factors such as trauma-related exposure, deployment length, and rank (Kok, Herrell, Thomas, & Hoge, 2012; Sundin et al., 2014), as well as methodological variations in sampling strategy and psychometrics (Creamer & Forbes, 2004; Rischardson, Frueh, & Acierno, 2010; Sundin, Fear, Iversen, Rona, & Wessely, 2010). (We have avoided providing comparisons across nations due to interpretational challenges).

Somewhat counterintuitively, PTSD prevalence is usually higher in ex-service populations than in currently serving cohorts (Stevelink et al., 2018; Van Hooff et al., 2018): since veterans are no longer exposed to military stressors, and should benefit

from the effects of a natural recovery process, one might expect PTSD rates to be lower in veterans. The explanation may lie in the additional stress faced by veterans as they swap the structure and security of the military for civilian life (e.g., finding jobs and accommodation, budgeting, and forming civilian relationships), which may provide time and space for past experiences (including traumatic events) to dominate consciousness. It may also be that personnel who develop substantial PTSD symptomology in service are more likely to leave resulting in higher rates of PTSD in the ex-service population. Research has also explored PTSD prevalence in specific military and veteran sub-populations, including peacekeepers (Souza et al., 2011) and military personnel (particularly women) who have experienced MST (Kimerling et al., 2010), with results showing significant levels of PTSD even in the absence of combat exposure.

Notwithstanding the heterogeneity in PTSD prevalence research, there is sufficient consistency to conclude that, in the majority of Western countries: a) PTSD remains one of the common mental disorders in both military and veteran populations; b) PTSD rates increase in proportion to potentially traumatic event exposure (including combat); and c) prevalence is higher among discharged veterans than among active duty military.

Questions of Causality: Risk indicators and risk factors for military-related PTSD

Risk factors are antecedents that contribute causally to the condition of interest, in this case PTSD, while risk indicators are characteristics of subgroups in whom the condition of interest is more common but where evidence of causality remains uncertain (American Psychiatric Association, 2013). PTSD appears to arise in individuals owing the interaction of multiple causal risk factors. While numerous risk indicators have been

identified, PTSD causality is not yet fully explained. Exposure to a traumatic event is required as part of the diagnostic criteria for PTSD. Yet, while PTSD is a common cause of morbidity in military and veteran populations, the majority of those exposed to potentially traumatic events do not develop PTSD. Thus, exposure to a traumatic event is a necessary but not sufficient risk factor in understanding individual risk for developing PTSD. The onset of PTSD is influenced by a complex interaction of biological, cognitive, and psychosocial factors across various time points. Research suggests that, as with civilians, a whole life approach to understanding risk for PTSD is required, since risk indicators have been identified in pre-trauma, peri-trauma, and post-trauma time periods (Brewin, Andrews, & Valentine, 2000). The person's stage of life and developmental tasks at the time of trauma exposures and recovery feed into this complex mix. In addition, the risk factors for the development of PTSD are not necessarily the same as the risk factors for chronicity (Schnurr, Lunney, & Sengupta, 2004).

Commonly cited pre-trauma risk indicators in military and veteran populations include age, gender, race, education, and military status (M. Jones et al., 2013; Xue et al., 2015). Research has consistently shown that childhood trauma is a significant risk factor for later development of PTSD and, as noted above, military and veteran populations are more likely to report adverse childhood experiences. Sleep problems are also associated with, or potentially an early marker for, development of PTSD both at pre- and post-deployment (Gehrman et al., 2013; Wang et al., 2018).

Aspects of military service independent of deployment may influence the risk of developing PTSD, with factors such as service branch, rank, quality of leadership, social support, and unit cohesion proving relevant (Anderson et al.; N. Jones et al., 2012; Wright, Kelsall, Sim, Clarke, & Creamer, 2013). Similarly, historical overviews

addressing the issue of combat motivation and breakdown suggest that broader consideration should be given to the influence of the group and the key social connections between serving personnel as an important moderator of vulnerability within the military and following discharge (Janowitz & Shils, 1948; Wessely, 2006). Wessely argues that risk of psychological injury increases when the primary relationships of small fighting units are poor or fractured, or the unit is rendered ineffective, and individuals become isolated and lose their sense of connection to a powerful group. This possibility is supported by social network analyses in civilian contexts that fractured social networks following trauma increases risk for PTSD (Bryant et al., 2016). Indeed, given that unit cohesion and leadership are integral to occupational health in the military (Adler & Castro, 2013), they provide a potential avenue for reducing the risk of PTSD and enhancing adjustment following exposure to potentially traumatic events.

Trauma related risk factors in military and veteran populations include the extent of exposures, length of deployments, time between deployments, and (in most cases) number of deployments (Bliese, Thomas, McGurk, McBride, & Castro, 2011; Rona et al., 2014), mirroring civilian research indicating the cumulative risk effects of repeated trauma exposure. Post-trauma risk factors include concurrent and subsequent life stressors and post-deployment support, both within and outside the military environment. This is particularly critical during the adaptation period during transition to civilian life.

PTSD is often associated with other health problems. Comorbidity of psychiatric disorders is common, particularly depression, anxiety disorders, and substance use disorders, with co-morbidity more the rule than the exception (Head et al., 2016; Smith, Goldstein, & Grant, 2016). Chronic physical health conditions, medically unexplained

somatic symptoms and chronic pain also are recognized PTSD risk indicators (NICE, 2018). However, the nature and direction of causal relationships between PTSD and physical health status remain largely unexplored (Gautam, Jain, Gautam, Vahia, & Grover, 2017; McFarlane, Lawrence-Wood, Van Hooff, Malhi, & Yehuda, 2017). Suicidal ideation and attempts, although not exclusively related to PTSD, have also been the focus of considerable attention in recent years (Naifeh, Mash, et al., 2018; Naifeh, Ursano, et al., 2018). Significant functional impairment is common in the form of problematic relationships, reduced social networks, and poorer employment outcomes (Rona et al., 2009; Schnurr et al., 2009).

The current status of PTSD treatments

Earlier international PTSD treatment guidelines consistently found trauma-focused cognitive behavioural therapies, such as Cognitive Processing Therapy (CPT), Prolonged Exposure (PE) and Eye-Movement Desensitization and Reprocessing (EMDR) to be the gold standard for treatment (Australian Centre for Posttraumatic Mental Health, 2013). More recent guidelines expand the number of treatments with high levels of evidence. For example, the guideline jointly developed by the Department of Veterans Affairs and the Department of Defense (2017) in the US gave the strongest recommendation to trauma-focused psychotherapies such as PE, CPT, and EMDR, but also included a range of additional therapies in this recommendation (e.g., written narrative exposure, Brief Eclectic Therapy). The recent update of the UK National Institute for Clinical Excellence (NICE) PTSD Guideline differs slightly in endorsing PE and CPT with the strongest recommendations but giving a slightly lower rating to EMDR specifically in relation to military veterans who have been traumatised as a result of combat, in view of the more limited evidence base for EMDR in this population (NICE, 2018). Taken together, the consistent findings across several

guidelines from different countries recommend that trauma focussed psychological interventions should be the first line treatment for PTSD.

PTSD guidelines and meta-analyses (e.g., N. Jones, Burdett, Green, & Greenberg, 2017; Lee et al., 2016) have generally reported smaller clinical effects in pharmacotherapy than trauma-focused interventions. Increasing attention, however, is now being paid to the methodologies of studies included in those reviews. For example, the meta-analysis of these comparisons by Lee et al. (2016), while supporting the use of trauma focused interventions as first line, recommended the need for more direct head to head research with specific agents, as well as the need to prioritise studies utilising active controls instead of waitlist or treatment-as-usual conditions (Lee et al., 2016). Consistent with this, new evidence indicating little difference between sertraline plus enhanced medication management, PE plus placebo, and PE plus sertraline (Rauch et al., 2018) suggests that, as the direct comparison evidence base firms, more nuanced recommendations will emerge. Despite this, all current guidelines continue to emphasise the role of medication and recommend its use, where indicated, in stabilisation or where first-line treatments are not available, not acceptable, or have not worked.

The intensive treatment outcome research efforts in recent years, using high-quality randomised controlled trials, is commendable. Regrettably, however, research suggests that military and veteran populations experience more modest treatment outcomes than civilians, with around two-thirds retaining their PTSD diagnosis after treatment with CPT or PE (Steenkamp, Litz, Hoge, & Marmar, 2015). In view of these modest outcomes, modifications to standardised treatment may be required in clinical practice to suit the specific presentation. Promising early results, for example, have been found in the treatment of moral injury with veterans (Litz, Lebowitz, Gray, & Nash,

2017). Similarly, although more research is required, it is reasonable to assume that the presence of significant dissociation would have implications for treatment (Frewen & Lanius, 2015). Interestingly, one study found that female veterans who met criteria for the dissociative subtype of PTSD had reduced, but still meaningful, response to PE (Wolf, Lunney, & Schnurr, 2016).

Challenges in providing evidence-based treatments

Significant challenges exist in delivering evidence-based treatments to military and veteran populations. Pathways to care comprise multiple steps, including acknowledging the problem, making a decision to enter treatment, accessing care, and remaining in treatment. A multitude of potential barriers to care exist at each step (Forbes et al., 2018). Some of the key challenges in delivering evidence-based treatments to military and veteran populations with PTSD include: a) engagement and retention in treatment; b) absence of defined benchmarks for assessing treatment progress and non-response; and c) clinician-related barriers including reluctance by some to work with veteran populations, capability and willingness to use evidence-based treatments, and degree of treatment fidelity. The section below expands on these key barriers to effective care, of which stigma is a prominent one, before providing a framework for future research in order to best respond to these challenges.

Treatment engagement

Elements of military culture and organisation, as well as individual factors, can make help-seeking and treatment engagement a challenge. Engaging in help-seeking behaviours, and the associated perceived vulnerability, can be experienced as antithetical to the warrior ethos universal to all militaries that prize self-reliance and strength in the face of adversity. Combined with a tendency to externalise, this may

make it difficult for military personnel and veterans to acknowledge problems even to themselves and, if they do acknowledge them, to refuse mental health care on the grounds that they would rather handle the problem on their own (Naifeh et al., 2016). Further research is needed to better untangle the complexity of this preference for self-management in order to increase help-seeking behaviours and modify the way in which services are delivered (Adler, Britt, Riviere, Kim, & Thomas, 2015).

A further concern for serving members (as well as some emergency responders) is that engaging in PTSD treatment may have a negative effect on career trajectory (Coleman, Stevelink, Hatch, Denny, & Greenberg, 2017; Iversen et al., 2011). Some of these concerns are well-founded, as certain mental health problems and medication use can result in being assessed as unfit to deploy. Other concerns, such as being treated differently by leadership or fellow unit members, may or may not be justified yet the broad issue of stigma is clearly relevant (Sharp et al., 2015). Cultures, beliefs, and behaviours around help-seeking that develop in military service may become ingrained, remaining after transition out of the military (Sharp et al., 2015). There is some evidence that stigma is not a 'fixed' entity and, indeed, may be highest whilst service personnel are on deployment (Osório, Jones, Fertout, & Greenberg, 2013). This may be because deployed personnel develop an adaptive strong 'operational mindset' which allows them to focus on the various challenging tasks they are required to undertake whilst deployed. Such a mindset is unlikely to include positive attitudes towards help-seeking. The concept of stigma relates both to 'self-stigma' (the individuals' own beliefs and agreement with stereotypes they perceive others apply to themselves), and 'anticipated public stigma' (the manner in which they believe they will be viewed by others) (Forbes et al., 2018; Hoge et al., 2004; McFarlane, Hodson, Van Hooff, & Davies, 2011). Both types may impede help-seeking behaviour.

The nature of PTSD itself may also impede engaging in treatment (Blais, Hoerster, Malte, Hunt, & Jakupcak, 2014). A cardinal feature of the disorder is avoidance and it is not unusual for people with PTSD to go to extreme lengths in order to avoid reminders of their traumatic experience. Many treatments for PTSD, of course, require people to do the exact opposite and to confront the memory of their traumatic experiences repeatedly, and in rich sensory detail. Thus, avoidance may contribute to failure to engage in treatment, early drop out, and a delayed return to treatment. Finally, involvement in adversarial liability and compensation processes can contribute to delays and interruptions in treatment, potentially undermining recovery. Any process that prolongs symptoms and disability arising from PTSD will reduce opportunities for the individual to modify, re-focus, or substantially change their vocational goals. Movements internationally toward non-liability approaches to health care (i.e., automatic approval for treatment without going through a lengthy claims process) have helped to separate treatment seeking from compensation, hopefully reducing this potential barrier to care.

Primary care (in both military and civilian contexts) deserves special mention, since this will be the first point of contact for many people with PTSD or other mental health conditions. PTSD recognition, and patient engagement, can present major challenges for primary care providers. PTSD may present in a wide variety of ways. It could, for example, be just one of many differential diagnoses of nonspecific symptoms or a masked factor complicating the care of physical health conditions. It could manifest as late onset, remote from psychologically traumatic events, or as complex PTSD in persons with ongoing psychologically traumatic stressors. As the health practitioner most likely to be delivering initial and ongoing care, as well as providing referrals for

specialist mental health care, primary care providers need to find ways to recognise possible PTSD among a potentially complex array of clinical presentations.

Treatment non-response

"Head to head" comparisons of veterans and civilian patients have not been conducted and conclusions, therefore, must be drawn with caution. Nevertheless, observation of clinical effect sizes in the treatment outcome literature from several countries (e.g., Australia, US, Canada) suggests a poorer treatment response among military personnel and veterans compared to other trauma populations (N. Jones et al., 2017). High comorbidity may be a contributing factor, with military PTSD associated with high levels of problematic anger, substance abuse, sleep disturbance and emotional numbing (Knowles, Sripada, Defever, & Rauch, 2018). Personality style and military training (good soldiers may not necessarily make good patients), trauma history, over-representation of males, and differences across service delivery systems may all play a part in these somewhat disappointing outcomes. Despite recognition of the complexity and poor treatment response in military and veteran PTSD, there is little evidence and guidance to support sound clinical decision making when an individual: a) has an atypical presentation; b) has a complex presentation including several comorbidities and/or psycho-social problems that challenge considerations in how to sequence treatment; and/or c) does not respond to first or second-line treatments.

One outstanding question in the field is how to correctly identify treatment-resistant PTSD. This contrasts with other disorders such as depression which have clearly developed heuristic definitions of treatment resistance (McFarlane, 2019) and have adopted clinical algorithms that guide clinicians through the decision-making process of 'next steps' when treatment is ineffective and a change of treatment plan is indicated (Gautam et al., 2017). Sippel and colleagues (2018) have recently offered

guidance on how to define treatment resistant PTSD, but evidence is needed to inform the appropriate action in the context of non-response to treatment. As noted below, recent moves towards personalised medicine may have relevance in this context.

Clinician-related barriers

The quality of the therapeutic relationship is a key factor in achieving positive outcomes. To work effectively with military and veteran populations, practitioners need an understanding of military culture and have the capacity to tolerate details of traumatic experiences whilst maintaining unconditional positive regard (Australian Centre for Posttraumatic Mental Health, 2013). In addition to consideration of the therapeutic relationship, the skills needed to deliver trauma-focused treatments are time-intensive and expensive to obtain. Research suggests that, even after a clinician has been appropriately trained in trauma-focused treatment, the uptake and implementation with military and veteran populations with PTSD is poor (Rosen et al., 2017; Rosen et al., 2016). There are several reasons why clinicians might be hesitant to use evidence based interventions, including doubts about the effectiveness of trauma-focused treatments and concerns about distressing the patient with recounting and recalling the traumatic memory.

Maintaining the fidelity of PTSD treatment protocols in real world clinical settings is always a challenge, as practitioners adapt the protocols to suit specific clinical presentations, including the unique features of military and veteran populations (Cook, Dinnen, Thompson, Simiola, & Schnurr, 2014). Perhaps not unreasonably, when veterans do not respond to first-line treatments, and in the absence of evidence-based clinical decision algorithms for treatment resistant PTSD, clinicians may seek alternative approaches to treatment. While some of these options may be clinically appropriate, others may be of little therapeutic benefit and there is a risk of long

treatment episodes that achieve little. As a result, implementation of treatments that work, as well as maintaining patients in these treatments, is becoming an increasing focus and cause for concern, in addition to concerns regarding the quality and impact of the treatments themselves (Sippel et al., 2018; Stirman et al., 2017).

Innovative solutions to PTSD treatment challenges

The current challenges in PTSD treatment require development of scientifically robust innovations that are consistent with the priorities of military personnel and veterans, and accessible to them across nations. We will now explore possible research directions necessary to progress this agenda over the next decade.

Agreed terminology and definitions

A clear consensus on what constitutes PTSD treatment success, treatment failure and/or non-response, treatment resistance, and cure and/or remission, along with an agreed terminology, is essential. A fundamental problem at present is how to operationalise when a person has had sufficient treatment. Varying definitions exist and are not used systematically across studies (Schnurr & Lunney, 2016; Sippel et al., 2018). Operationalisation of these constructs will facilitate development of clinical algorithms to guide decision making and treatment planning in cases of treatment non-response, treatment resistance, or relapse.

Strategies to increase engagement

Strategies to enhance engagement include increasing individual awareness of the need for treatment, reducing stigma, alternative methods of healthcare delivery, enhancing treatment acceptability and accessibility, and involving families, military leaders and communities in sustaining an environment supportive of care. A better

understanding of the many steps in the pathway to care is needed in order to effectively target strategies to increase engagement at all levels. These improvements could be facilitated through leadership initiatives, unit-based bystander support, and family involvement, as well as through strategies designed to increase awareness of the benefits of PTSD treatment.

Systemic changes are required to improve the coordination and integration of healthcare services within and between military and veteran systems, as well as to improve accessibility, quality, and resourcing of those services. Such systemic improvements are particularly important during key transition periods. The organisational culture needs to actively promote engagement in treatment when required, from the highest levels of leadership through various command levels, to leveraging unit and "buddy" support. Peers (i.e., "buddies" and "mates") can be particularly important in encouraging engagement in care. Emerging research examining the effectiveness of peer led engagement and help promoting activities following exposures are demonstrating promise and warrant further investigation (N. Jones et al., 2017).

Identifying who will benefit from intervention is a key component of engagement. While population screening has been considered, large automated screening trials have demonstrated little impact on treatment seeking (Rona et al., 2017). Face to face engagement with healthcare professionals, often including education and some psychometric screening, is currently delivered in several Defence Forces, with the goal of facilitating early detection, case identification, and engagement in treatment if required. Such approaches are commonly applied to cohorts at specific timepoints (e.g., following deployment, at the point of transition) and, when indicated, in primary care settings. Studies building on the work of Rona et al. (2017) to examine the

effectiveness of different elements provided in current face to face engagement and screening practices are critical to ensure that scarce resources are devoted to where the gains will be most substantial (McFarlane 2017). An integrated approach to identifying mental health problems, which may include screening across the deployment cycle is needed to facilitate continuity of care from garrison to deployment and back again (Warner, Appenzeller, Parker, Warner, & Hoge, 2011).

On a related theme, it may be possible to go beyond screening based purely on self-report to explore other risk markers. While military personnel can develop PTSD after a single incident during service, there is increasing recognition that repeated deployments confer an incremental risk of developing PTSD (McFarlane et al., 2011). Conceptualising PTSD within a staging model, whereby trauma exposed individuals have not developed symptoms but are at greater risk due to high likelihood of further exposure and are presenting with certain biomarkers, may provide opportunity for early engagement and avoid the complications, comorbidity, and psychosocial losses associated with chronicity and a prolonged recovery process (McFarlane et al., 2017). It is unclear, however, how effective these interventions might be in returning personnel to full function and studies are required to properly understand the occupational prognosis of trauma-related adjustment disorders which develop during service, with or without early intervention.

Collaborative care models in primary care (e.g., a multidisciplinary team approach), which have a strong evidence base in mental health (Archer et al., 2012), may assist with increasing engagement in PTSD treatment, helping to efficiently identify PTSD patients and match care according to clinical complexity and patient characteristics (Engel et al., 2016). Emerging evidence around case management has significant promise for high risk and complex cases (Kehle-Forbes & Kimerling, 2017).

However, trials of collaborative care for PTSD have yielded mixed results, and point to the importance of ensuring that collaborative care involves effective treatments (Schnurr, 2016; Schnurr et al., 2013).

Modifications to PTSD treatments or healthcare service structures also have the potential to increase military and veteran engagement with PTSD treatment. Massed treatment, for example, such as intensive PE (Foa et al., 2018) and CPT or CT (Ehlers et al., 2014), may be appealing to military personnel who may have limited availability for lengthy treatment periods. Another potential treatment modification, designed to improve maintenance of treatment gains, is booster sessions after treatment completion. Little evidence is available regarding the long-term benefits of treatment for PTSD because most trials only assess outcomes in the short and medium term, but the few long term follow-ups that exist suggest initial treatment gains may not be maintained over time (Resick, Williams, Suvak, Monson, & Gradus, 2012; Shalev et al., 2016). Booster sessions may provide beneficial refresher training of skills taught in therapy, and lead to greater symptom reduction in the long-term. In addition, continued expansion of telehealth and related modalities may assist in making evidence-based treatment, educational activities, and research participation more accessible.

Improved understanding of treatment outcome predictors

Research focused on uncovering predictors of treatment outcome, including active facilitators and inhibitors of change, is vital. Loss, shame, and problematic anger are particularly relevant to military and veteran populations and have been demonstrated to be potentially important inhibitors of treatment outcomes (Forbes et al., 2005; Lloyd et al., 2014; Yehuda, Vermetten, McFarlane, & Lehrner, 2014). There is mixed evidence around the extent to which depression, guilt, anxiety, and dissociation at pre-

treatment are associated with poorer treatment response (e.g., Richardson et al., 2014). Recent research has suggested that it may be a combination of co-occurring risk indicators that best predicts outcomes (e.g., severe PTSD, guilt and depression as a co-occurring triad) rather than single predictors considered independently (Phelps et al., 2018). Further work is needed in developing the evidence base around differential treatment response in individual PTSD profiles with a view to evidence based guidelines for treatment sequencing and the development of interventions for clusters of features such as the triad outlined above. The emerging concept of moral injury and its implications for PTSD interventions is also relevant here (Bryan, Bryan, Roberge, Leifker, & Rozek, 2017). Different approaches might be required when the impact of traumatic experiences manifests as recognisable symptoms of PTSD (e.g., arousal) but the mechanism of action driving symptoms is markedly different (e.g., not fear of harm but beliefs about transgressions of core beliefs or perceived betrayals by self or others – moral injury; Williamson, Stevelink, & Greenberg, 2018).

Innovations in treatment

Now that the evidence base for first-line treatments of PTSD is established, increasing attention is being paid to related questions. The following are important areas for further research: a) how to improve, complement, and augment current evidence-based treatments to maximise treatment response; b) expanding knowledge about non-trauma focused treatments; c) novel pharmacotherapy; d) personalised medicine approaches; and e) treatments that specifically aim to enhance functioning.

i) Enhancing existing treatments

Research must continue to focus on strategies designed to prepare an individual for treatment, better engage an individual in treatment, or augment the effects of current treatments. Advances in neuroscience, cognitive psychology and pharmacology have

produced several novel approaches to augmenting current PTSD treatments that can be used concurrently with trauma-focused treatments or in a preparatory fashion. Examples include pharmacological approaches such as MDMA, ketamine, and LSD, which, when used in conjunction with unstructured psychotherapy, may facilitate engagement with the traumatic memory (Mithoefer, Grob, & Brewerton, 2016). Further work is also underway in combining MDMA with evidence based trauma focused treatments. The use of propranolol, a noradrenergic beta-receptor blocker, as a putative reconsolidation blocker in conjunction with psychotherapy also shows some promise in reducing PTSD symptoms (Brunet et al., 2018).

Recent developments in cognitive and neuroscientific interventions that aim to enhance working memory or improve attention control (McDermott et al., 2016), transcranial magnetic stimulation (TMS; Kozel et al., 2019), and new technologies such as virtual reality (Reger et al., 2016) have also shown promise as augmentation interventions.

Given the evidence indicating that anger inhibits treatment response in PTSD, using targeted anger interventions in a phased approach prior to trauma focused treatment may offer benefit (Cash et al., 2018). Experiential and physical treatments such as physical exercise or creative art therapies, and current second-line treatments such as acupuncture or mindfulness, may have a role to play in augmenting existing first line treatments (as well as potentially treatments in their own right). While these approaches may be more acceptable to some service members, their effects on improving PTSD are not well studied (Benedek & Wynn, 2016).

ii) Non-trauma-focused treatments

Current promising non-trauma-focused treatments for PTSD include Interpersonal therapy (Markowitz et al., 2015), Mindfulness-Based Stress Reduction

(Polusny et al., 2015), and Present-Centred Therapy (Schnurr et al., 2007), which was initially conceptualised as a control treatment. Emerging evidence in neurofeedback and biofeedback is also showing promise (Fisher, Lanius, & Frewen, 2016). As noted above, although it is not yet known whether these non-trauma focus interventions will improve outcomes for military personnel or veterans who do not respond to first-line treatments, they may be more acceptable to those who express a strong preference not to engage in trauma focused work. Similarly, in recognition that PTSD is often comorbid with other psychiatric disorders, transdiagnostic approaches are becoming increasingly considered as a useful approach for trauma related pathology (Gutner, Galovski, Bovin, & Schnurr, 2016).

iii) Novel pharmacotherapy

A common theme in recent literature is the disappointing lack of innovation in the development of effective pharmacotherapy for PTSD (Krystal et al., 2017). Antidepressants targeting traditional monaminergic systems, in particular selective serotonin reuptake inhibitors, remain the first line evidence-based treatments when considering medications. Given the limited effect size of agents like the SSRIs (Ipser & Stein, 2012) and the absence of a PTSD-specific agent, a range of agents predominantly designed for other mental health conditions have also been trialled or frequently utilized including other antidepressant, anxiolytic and antipsychotic medications. At this point, none have reached established high level evidence. Work is currently underway, however, focussing on non-monoaminergic transmitter systems that may be of specific relevance to the neurobiology of PTSD. A recent expert consensus identified a list of mechanisms that should be targeted for ongoing research, with the top three being NMDA receptor antagonists, cannabinoid receptor modulators, and glucocorticoid receptor agonists (Krystal et al., 2017).

iv) Personalised medicine

Personalised medicine in PTSD, where treatments are tailored to match the specific needs of an individual military member or veteran, holds considerable promise. This work now goes well beyond the traditional genomic focus of personalised medicine. Research is needed on how to improve treatment fit and effectiveness through better understanding of the typologies of PTSD phenotypes and across the biopsychosocial indicators. Advances in use of fMRI, EEG, biomarkers and genetics hold some promise also for improved understanding of neurobiological profile variations and the for potential matching and tailoring interventions. In addition, large randomised controlled trial datasets using first-line treatments such as PE and CPT (Schnurr et al., 2015) could form a base for machine learning approaches to identify which interventions work for whom. This "big data" research can then drive appropriate adaptations to the treatment protocols or the clinical setting and provide informed guidance for treatment selection through data-driven, continuous quality improvement (Cook et al., 2014). Machine learning approaches to large data may aid in moving PTSD to personalized medicine, matching the individual with the most likely successful treatment.

v) Approaches specifically designed to enhance functioning

Since PTSD is routinely associated with impaired social and occupational functioning, it is critical to develop and rigorously evaluate interventions designed to have a broader social-occupational focus on wellbeing and function (examples include not only occupational rehabilitation, but also support animals, equine therapy, and hiking). Such interventions have the potential to provide avenues to engagement in activity, positive social connections and regaining a sense of self beyond the mental health problems. Indeed, such interventions may succeed where traditional approaches

have been unsuccessful, including in preparatory phases prior to first line treatments. In the absence of robust evidence, however, it is important that these approaches are not considered as a substitute for evidence based interventions. Psychological wellbeing is strongly influenced by participation in life roles, but ensuring role participation requires: (a) recognising, diagnosing and effectively treating the condition so as to minimize impairments; (b) enabling adaptive coping for those living with the condition; and (c) reducing barriers to role participation in their social and physical environments.

vi) The role of family intervention and support

While the impact on families is beyond the scope of this paper, it is nevertheless important to recognise the difficulties faced by family members of military personnel and veterans with PTSD. How do we care for the wellbeing of families as an end goal in of itself, and how do we improve their wellbeing in a way that supports the veteran's recovery? Research consistently finds that support and encouragement from loved ones increases treatment initiation and retention in military and veteran populations (Murphy, Palmer, Hill, Ashwick, & Busuttil, 2017). The burden of care shouldered by the families of those with PTSD is substantial and the impact on their own mental health needs must be assessed in order to minimise long term negative consequences for the PTSD sufferer and the family (Cramm, Mahar, MacLean, & Birtwhistle, 2019; Fear et al., 2018).

vii) Attention to physical health

Specialist mental health providers and researchers are sometimes at risk of focussing exclusively on psychiatric conditions and ignoring the role of chronic physical health conditions, medically unexplained symptoms, and chronic pain. Those three types of problems are disproportionately prevalent in persons with PTSD (as, indeed, they are in persons with depression or anxiety disorders). Whole person

management must include attention to comorbid/co-occurring physical health problems in addition to the psychiatric condition (Sharp, 2019).

Strengths and Weaknesses

The author group of this paper was convened by the 5 Eyes Mental Health Research and Innovation Collaborative (5 Eyes MHRIC). The 5 Eyes MHRIC is a collaboration of mental health researchers in Canada, Australia, the United States, the United Kingdom and New Zealand working to improve mental health outcomes for past and present military personnel and their families. The paper reflects interpretations of the evidence base by a group of researchers working on military and veteran mental health in those countries and might not represent the views of other researchers. However, the broad representation of disciplines, nationalities and military and veteran life course stages mitigates the risks of bias.

Summary and Conclusions

Research over the past decade has demonstrated that evidence-based treatments, when used correctly, can be moderately effective for treating PTSD in military and veteran populations. Improvements in symptom reduction and quality of life for some individuals are modest, however, highlighting the need for improved PTSD treatment and chronic symptom management approaches.

This paper has provided an overview of key questions in each of several important areas for future research including: a) developing a consensus on terminology and definitions around treatment success, failure and/or non-response, resistance, and cure/remission; b) developing individual and systemic approaches to enhancing treatment engagement, including addressing stigma, improving early recognition, and modifying treatment; c) improving our understanding of predictors of treatment

outcome; d) improving the efficacy of treatment through enhancing existing interventions, exploring new approaches, increasing personalised approaches to treatment, and increasing the focus on functional impairment and physical health.

We also do not underestimate the scale of this important task. We also recognise that research directions will continue to be driven, in large part, by the individual interests of researchers, by the availability of targeted research funding, and by various social and government priorities. Nevertheless, we believe that the future directions outlined in this paper will inform key developments in each of the nominated areas. The authorship group is are committed to ongoing international collaboration with a view to optimising a consistent and coherent approach to research and policy in military and veteran mental health.

The agenda for future research needs to be ambitious, focussing on international cooperation and extending the focus beyond a "one-size-fits-all" approach in order to tailor treatment to individual need. Only then will we ensure better mental health outcomes for serving personnel, veterans, and their families.

References

Adler, A. B., Britt, T. W., Riviere, L. A., Kim, P. Y., & Thomas, J. L. (2015). Longitudinal determinants of mental health treatment-seeking by US soldiers. *The British Journal of Psychiatry, 207*(4), 346-350.

Adler, A. B., & Castro, C. A. (2013). An occupational mental health model for the military. *Military Behavioral Health, 1*(1), 41-45.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Washington DC: American Psychiatric Association.

Andersen, J., Wade, M., Possemato, K., & Ouimette, P. (2010). Association between posttraumatic stress disorder and primary care provider-diagnosed disease among Iraq and Afghanistan veterans. *Psychosomatic Medicine, 72*(5), 498-504.

Anderson, L., Campbell-Sills, L., Ursano, R. J., Kessler, R. C., Sun, X., Heeringa, S. G., . . . Stein, M. B. (2019). Prospective associations of perceived unit cohesion with postdeployment mental health outcomes. *Depression and anxiety, 0*(0). doi: doi:10.1002/da.22884

Archer, J., Bower, P., Gilbody, S., Lovell, K., Richards, D., Gask, L., . . . Coventry, P. (2012). Collaborative care for depression and anxiety problems. *Cochrane Database of Systematic Reviews*(10).

Australian Centre for Posttraumatic Mental Health. (2013). *Australian Guidelines for the Treatment of Acute Stress Disorder and Posttraumatic Stress Disorder*. Melbourne, Victoria: ACPMH.

Benedek, D. M., & Wynn, G. H. (2016). *Complementary and alternative medicine for PTSD*: Oxford University Press.

Blais, R. K., Hoerster, K. D., Malte, C., Hunt, S., & Jakupcak, M. (2014). Unique PTSD clusters predict intention to seek mental health care and subsequent utilization in US veterans with PTSD symptoms. *Journal of traumatic stress, 27*(2), 168-174.

Bliese, P. D., Thomas, J. L., McGurk, D., McBride, S., & Castro, C. A. (2011). Mental health advisory teams: a proactive examination of mental health during combat deployments. *International Review of Psychiatry, 23*(2), 127-134.

Blosnich, J. R., Dichter, M. E., Cerulli, C., Batten, S. V., & Bossarte, R. M. (2014). Disparities in adverse childhood experiences among individuals with a history of military service. *JAMA psychiatry, 71*(9), 1041-1048.

Brewin, C. R., Andrews, B., & Valentine, J. D. (2000). Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. *Journal of consulting and clinical psychology, 68*(5), 748.

Bruffaerts, R., Vilagut, G., Demyttenaere, K., Alonso, J., AlHamzawi, A., Andrade, L. H., . . . De Girolamo, G. (2012). Role of common mental and physical disorders in partial disability around the world. *The British Journal of Psychiatry*.

Brunet, A., Saumier, D., Liu, A., Streiner, D. L., Tremblay, J., & Pitman, R. K. (2018). Reduction of PTSD symptoms with pre-reactivation propranolol therapy: a randomized controlled trial. *American Journal of Psychiatry, 175*(5), 427-433.

Bryan, C. J., Bryan, A. O., Roberge, E., Leifker, F. R., & Rozek, D. C. (2017). Moral injury, posttraumatic stress disorder, and suicidal behavior among National Guard personnel.

Bryant, R. A., Gallagher, H. C., Gibbs, L., Pattison, P., MacDougall, C., Harms, L., . . . Ireton, G. (2016). Mental health and social networks after disaster. *American Journal of Psychiatry, 174*(3), 277-285.

Cash, R., Varker, T., McHugh, T., Metcalf, O., Howard, A., Lloyd, D., . . . Forbes, D. (2018). Effectiveness of an anger intervention for military members with PTSD: a clinical case series. *Military medicine*.

Chapman, C., Mills, K., Slade, T., McFarlane, A. C., Bryant, R., Creamer, M., . . . Teesson, M. (2012). Remission from post-traumatic stress disorder in the general population. *Psychological medicine, 42*(8), 1695-1703.

Coleman, S., Stevelink, S., Hatch, S., Denny, J., & Greenberg, N. (2017). Stigma-related barriers and facilitators to help seeking for mental health issues in the armed forces: a systematic review and thematic synthesis of qualitative literature. *Psychological medicine, 47*(11), 1880-1892.

Cook, J. M., Dinnen, S., Thompson, R., Simiola, V., & Schnurr, P. P. (2014). Changes in implementation of two evidence-based psychotherapies for PTSD in VA residential treatment programs: A national investigation. *Journal of traumatic stress, 27*(2), 137-143.

Cramm, H., Mahar, A., MacLean, C., & Birtwhistle, R. (2019). Caring for Canadian military families. *Canadian Family Physician, 65*(1), 9-11.

Creamer, M., & Forbes, D. (2004). Treatment of posttraumatic stress disorder in military and veteran populations. *Psychotherapy: Theory, Research, Practice, Training, 41*(4), 388.

Ehlers, A., Hackmann, A., Grey, N., Wild, J., Liness, S., Albert, I., . . . Clark, D. M. (2014). A randomized controlled trial of 7-day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. *American Journal of Psychiatry, 171*(3), 294-304.

Engel, C. C., Jaycox, L. H., Freed, M. C., Bray, R. M., Brambilla, D., Zatzick, D., . . . Lane, M. E. (2016). Centrally assisted collaborative telecare for posttraumatic stress disorder and depression among military personnel attending primary care: a randomized clinical trial. *JAMA internal medicine, 176*(7), 948-956.

Fear, N. T., Reed, R. V., Rowe, S., Burdett, H., Pernet, D., Mahar, A., . . . Wessely, S. (2018). Impact of paternal deployment to the conflicts in Iraq and Afghanistan and paternal post-traumatic stress disorder on the children of military fathers. *The British Journal of Psychiatry, 212*(6), 347-355.

Fisher, S. F., Lanius, R. A., & Frewen, P. A. (2016). EEG neurofeedback as adjunct to psychotherapy for complex developmental trauma-related disorders: Case study and treatment rationale. *Traumatology, 22*(4), 255.

Foa, E. B., McLean, C. P., Zang, Y., Rosenfield, D., Yadin, E., Yarvis, J. S., . . . Dondanville, K. A. (2018). Effect of prolonged exposure therapy delivered over 2 weeks vs 8 weeks vs present-centered therapy on PTSD symptom severity in military personnel: A randomized clinical trial. *Jama, 319*(4), 354-364.

Forbes, D., Bennett, N., Biddle, D., Crompton, D., McHugh, T., Elliott, P., & Creamer, M. (2005). Clinical presentations and treatment outcomes of peacekeeper veterans with PTSD: Preliminary findings. *American Journal of Psychiatry, 162*(11), 2188-2190.

Forbes, D., Van Hooff, M., Lawrence-Wood, E., Sadler, N., Hodson, S., Benassi, H., . . . McFarlane, A. (2018). *The Transition & Wellbeing Research Programme: Mental Health and Wellbeing Transition Study. Report 2: Pathways to Care.* . Canberra.

Frewen, P., & Lanius, R. (2015). *Healing the traumatized self: Consciousness, neuroscience, treatment. 2015*. New York, New York: WW Norton and Company.

Gautam, S., Jain, A., Gautam, M., Vahia, V. N., & Grover, S. (2017). Clinical practice guidelines for the management of depression. *Indian journal of psychiatry, 59*(Suppl 1), S34.

Gehrman, P., Seelig, A. D., Jacobson, I. G., Boyko, E. J., Hooper, T. I., Gackstetter, G. D., . . . Team, M. C. S. (2013). Predeployment sleep duration and insomnia symptoms as risk factors for new-onset mental health disorders following military deployment. *Sleep, 36*(7), 1009-1018.

Gutner, C. A., Galovski, T., Bovin, M. J., & Schnurr, P. P. (2016). Emergence of transdiagnostic treatments for PTSD and posttraumatic distress. *Current psychiatry reports, 18*(10), 95.

Head, M., Goodwin, L., Debell, F., Greenberg, N., Wessely, S., & Fear, N. (2016). Post-traumatic stress disorder and alcohol misuse: comorbidity in UK military personnel. *Social psychiatry and psychiatric epidemiology, 51*(8), 1171-1180.

Hoge, C. W., Castro, C. A., Messer, S. C., McGurk, D., Cotting, D. I., & Koffman, R. L. (2004). Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *New England Journal of Medicine, 351*(1), 13-22.

Ipser, J. C., & Stein, D. J. (2012). Evidence-based pharmacotherapy of post-traumatic stress disorder (PTSD). *International Journal of Neuropsychopharmacology, 15*(6), 825-840.

Iversen, A. C., van Staden, L., Hughes, J. H., Greenberg, N., Hotopf, M., Rona, R. J., . . . Fear, N. T. (2011). The stigma of mental health problems and other barriers to care in the UK Armed Forces. *BMC health services research, 11*(1), 31.

Janowitz, M., & Shils, E. (1948). Cohesion and disintegration in the Wehrmacht in World War II. *Public Opinion Quarterly, 12*(2), 280-315.

Jones, M., Sundin, J., Goodwin, L., Hull, L., Fear, N. T., Wessely, S., & Rona, R. (2013). What explains post-traumatic stress disorder (PTSD) in UK service personnel: deployment or something else? *Psychological medicine, 43*(8), 1703-1712.

Jones, N., Burdett, H., Green, K., & Greenberg, N. (2017). Trauma Risk Management (TRiM): Promoting Help Seeking for Mental Health Problems Among Combat-Exposed UK Military Personnel. *Psychiatry, 80*(3), 236-251.

Jones, N., Seddon, R., Fear, N. T., McAllister, P., Wessely, S., & Greenberg, N. (2012). Leadership, cohesion, morale, and the mental health of UK Armed Forces in Afghanistan. *Psychiatry: Interpersonal & Biological Processes, 75*(1), 49-59.

Kehle-Forbes, S., & Kimerling, R. (2017). Patient engagement in PTSD treatment. *PTSD Research Quarterly, 28*(3).

Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012). Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *International journal of methods in psychiatric research, 21*(3), 169-184.

Kimerling, R., Street, A. E., Pavao, J., Smith, M. W., Cronkite, R. C., Holmes, T. H., & Frayne, S. M. (2010). Military-related sexual trauma among Veterans Health Administration patients returning from Afghanistan and Iraq. *American journal of public health, 100*(8), 1409-1412.

Knowles, K. A., Sripada, R. K., Defever, M., & Rauch, S. A. (2018). Comorbid mood and anxiety disorders and severity of posttraumatic stress disorder symptoms in treatment-seeking veterans. *Psychological Trauma: Theory, Research, Practice, and Policy*.

Kok, B. C., Herrell, R. K., Thomas, J. L., & Hoge, C. W. (2012). Posttraumatic stress disorder associated with combat service in Iraq or Afghanistan: reconciling

prevalence differences between studies. *The Journal of nervous and mental disease, 200*(5), 444-450.

Kozel, F. A., Van Trees, K., Larson, V., Phillips, S., Hashimie, J., Gadbois, B., . . . Toyinbo, P. (2019). One Hertz versus Ten Hertz repetitive TMS treatment of PTSD: A Randomized Clinical Trial. *Psychiatry research*.

Krystal, J. H., Davis, L. L., Neylan, T. C., Raskind, M. A., Schnurr, P. P., Stein, M. B., . . . Huang, G. D. (2017). It is time to address the crisis in the pharmacotherapy of posttraumatic stress disorder: a consensus statement of the PTSD Psychopharmacology Working Group. *Biological psychiatry, 82*(7), e51-e59.

Lee, D. J., Schnitzlein, C. W., Wolf, J. P., Vythilingam, M., Rasmusson, A. M., & Hoge, C. W. (2016). Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: Systemic review and meta-analyses to determine first-line treatments. *Depression and anxiety, 33*(9), 792-806.

Litz, B. T., Lebowitz, L., Gray, M. J., & Nash, W. P. (2017). *Adaptive disclosure: A new treatment for military trauma, loss, and moral injury*: Guilford Publications.

Lloyd, D., Nixon, R., Varker, T., Elliott, P., Perry, D., Bryant, R., . . . Forbes, D. (2014). Comorbidity in the prediction of cognitive processing therapy treatment outcomes for combat-related posttraumatic stress disorder. *Journal of anxiety disorders, 28*(2), 237-240.

Maercker, A., Brewin, C. R., Bryant, R. A., Cloitre, M., van Ommeren, M., Jones, L. M., . . . Rousseau, C. (2013). Diagnosis and classification of disorders specifically associated with stress: proposals for ICD-11. *World Psychiatry, 12*(3), 198-206.

Magruder, K. M., & Yeager, D. E. (2009). The prevalence of PTSD across war eras and the effect of deployment on PTSD: A systematic review and meta-analysis. *Psychiatric Annals, 39*(8).

Markowitz, J. C., Petkova, E., Neria, Y., Van Meter, P. E., Zhao, Y., Hembree, E., . . . Marshall, R. D. (2015). Is exposure necessary? A randomized clinical trial of interpersonal psychotherapy for PTSD. *American Journal of Psychiatry, 172*(5), 430-440.

McDermott, T. J., Badura-Brack, A. S., Becker, K. M., Ryan, T. J., Bar-Haim, Y., Pine, D. S., . . . Wilson, T. W. (2016). Attention training improves aberrant neural dynamics during working memory processing in veterans with PTSD. *Cognitive, Affective, & Behavioral Neuroscience, 16*(6), 1140-1149.

McFarlane, A. (2019). Treatment Resistance in Post-traumatic Stress Disorder *Treatment Resistance in Psychiatry* (pp. 151-164): Springer.

McFarlane, A., Hodson, S., Van Hooff, M., & Davies, C. (2011). *Mental health in the Australian Defence Force: 2010 ADF Mental Health and Wellbeing Study: Full report.* Canberra.

McFarlane, A., Lawrence-Wood, E., Van Hooff, M., Malhi, G. S., & Yehuda, R. (2017). The need to take a staging approach to the biological mechanisms of PTSD and its treatment. *Current psychiatry reports, 19*(2), 10.

Mithoefer, M. C., Grob, C. S., & Brewerton, T. D. (2016). Novel psychopharmacological therapies for psychiatric disorders: psilocybin and MDMA. *The Lancet Psychiatry, 3*(5), 481-488.

Murphy, D., Palmer, E., Hill, K., Ashwick, R., & Busuttil, W. (2017). Living alongside military PTSD: a qualitative study of female partners' experiences with UK Veterans. *Journal of Military, Veteran and Family Health, 3*(1), 52-61.

Naifeh, J. A., Colpe, L. J., Aliaga, P. A., Sampson, N. A., Heeringa, S. G., Stein, M. B., . . . Schoenbaum, M. (2016). Barriers to initiating and continuing mental health treatment among soldiers in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). *Military medicine, 181*(9), 1021-1032.

Naifeh, J. A., Mash, H. B. H., Stein, M. B., Fullerton, C. S., Kessler, R. C., & Ursano, R. J. (2018). The Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS): progress toward understanding suicide among soldiers. *Molecular psychiatry*, 1.

Naifeh, J. A., Ursano, R. J., Kessler, R. C., Zaslavsky, A. M., Nock, M. K., Dempsey, C. L., . . . Zuromski, K. L. (2018). Transition to suicide attempt from recent suicide ideation in US Army soldiers: Results from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). *Depression and anxiety*.

NICE. (2018). *Post-traumatic stress disorder, NICE Guideline [NG116]*.

O'Toole, B. I., Catts, S. V., Outram, S., Pierse, K. R., & Cockburn, J. (2009). The physical and mental health of Australian Vietnam veterans 3 decades after the war and its relation to military service, combat, and post-traumatic stress disorder. *American Journal of Epidemiology, 170*(3), 318-330.

Osório, C., Jones, N., Fertout, M., & Greenberg, N. (2013). Perceptions of stigma and barriers to care among UK military personnel deployed to Afghanistan and Iraq. *Anxiety, Stress & Coping, 26*(5), 539-557.

Phelps, A., Steel, Z., Metcalf, O., Alkemade, N., Kerr, K., O'donnell, M., . . . Armstrong, R. (2018). Key patterns and predictors of response to treatment for military veterans with post-traumatic stress disorder: a growth mixture modelling approach. *Psychological medicine, 48*(1), 95-103.

Polusny, M. A., Erbes, C. R., Thuras, P., Moran, A., Lamberty, G. J., Collins, R. C., . . . Lim, K. O. (2015). Mindfulness-based stress reduction for posttraumatic stress disorder among veterans: a randomized clinical trial. *Jama, 314*(5), 456-465.

Prigerson, H. G., Maciejewski, P. K., & Rosenheck, R. A. (2001). Combat trauma: trauma with highest risk of delayed onset and unresolved posttraumatic stress disorder symptoms, unemployment, and abuse among men. *The Journal of nervous and mental disease, 189*(2), 99-108.

Rauch, S. A., Kim, H. M., Powell, C., Tuerk, P. W., Simon, N. M., Acierno, R., . . . Rothbaum, B. O. (2018). Efficacy of Prolonged Exposure Therapy, Sertraline Hydrochloride, and Their Combination Among Combat Veterans With Posttraumatic Stress Disorder: A Randomized Clinical Trial. *JAMA psychiatry*.

Reger, G. M., Koenen-Woods, P., Zetocha, K., Smolenski, D. J., Holloway, K. M., Rothbaum, B. O., . . . Skopp, N. A. (2016). Randomized controlled trial of prolonged exposure using imaginal exposure vs. virtual reality exposure in active duty soldiers with deployment-related posttraumatic stress disorder (PTSD). *Journal of consulting and clinical psychology, 84*(11), 946.

Resick, P. A., Williams, L. F., Suvak, M. K., Monson, C. M., & Gradus, J. L. (2012). Long-term outcomes of cognitive–behavioral treatments for posttraumatic stress disorder among female rape survivors. *Journal of consulting and clinical psychology, 80*(2), 201.

Richardson, J. D., Contractor, A. A., Armour, C., St, K. C., Elhai, J. D., & Sareen, J. (2014). Predictors of long-term treatment outcome in combat and peacekeeping veterans with military-related PTSD. *The Journal of clinical psychiatry, 75*(11), e1299-1305.

Rischardson, L., Frueh, B., & Acierno, R. (2010). Prevalence estimates of combat-related PTSD: a critical review. *Australian & New Zealand Journal of Psychiatry, 44*, 4-19.

Rona, R. J., Burdett, H., Khondoker, M., Chesnokov, M., Green, K., Pernet, D., . . . Fear, N. T. (2017). Post-deployment screening for mental disorders and tailored advice about help-seeking in the UK military: a cluster randomised controlled trial. *The Lancet, 389*(10077), 1410-1423.

Rona, R. J., Jones, M., Iversen, A., Hull, L., Greenberg, N., Fear, N. T., . . . Wessely, S. (2009). The impact of posttraumatic stress disorder on impairment in the UK military at the time of the Iraq war. *Journal of psychiatric research, 43*(6), 649-655.

Rona, R. J., Jones, M., Keeling, M., Hull, L., Wessely, S., & Fear, N. T. (2014). Mental health consequences of overstretch in the UK Armed Forces, 2007–09: a population-based cohort study. *The Lancet Psychiatry, 1*(7), 531-538.

Rosen, C., Eftekhari, A., Crowley, J. J., Smith, B. N., Kuhn, E., Trent, L., . . . Ruzek, J. I. (2017). Maintenance and reach of exposure psychotherapy for posttraumatic stress disorder 18 months after training. *Journal of traumatic stress, 30*(1), 63-70.

Rosen, C., Matthieu, M., Stirman, S. W., Cook, J., Landes, S., Bernardy, N., . . . Finley, E. (2016). A review of studies on the system-wide implementation of evidence-based psychotherapies for posttraumatic stress disorder in the Veterans Health Administration. *Administration and Policy in Mental Health and Mental Health Services Research, 43*(6), 957-977.

Schnurr, P. P. (2016). Extending collaborative care for posttraumatic mental health. *JAMA internal medicine, 176*(7), 956-957.

Schnurr, P. P., Chard, K. M., Ruzek, J. I., Chow, B. K., Shih, M.-C., Resick, P. A., . . . Lu, Y. (2015). Design of VA Cooperative Study# 591: CERV-PTSD, comparative effectiveness research in veterans with PTSD. *Contemporary clinical trials, 41*, 75-84.

Schnurr, P. P., Friedman, M. J., Engel, C. C., Foa, E. B., Shea, M. T., Chow, B. K., . . . Haug, R. (2007). Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. *Jama, 297*(8), 820-830.

Schnurr, P. P., Friedman, M. J., Oxman, T. E., Dietrich, A. J., Smith, M. W., Shiner, B., . . . Thurston, V. (2013). RESPECT-PTSD: re-engineering systems for the primary care treatment of PTSD, a randomized controlled trial. *Journal of general internal medicine, 28*(1), 32-40.

Schnurr, P. P., & Lunney, C. A. (2016). Symptom benchmarks of improved quality of life in PTSD. *Depression and anxiety, 33*(3), 247-255.

Schnurr, P. P., Lunney, C. A., Bovin, M. J., & Marx, B. P. (2009). Posttraumatic stress disorder and quality of life: extension of findings to veterans of the wars in Iraq and Afghanistan. *Clinical Psychology Review, 29*(8), 727-735.

Schnurr, P. P., Lunney, C. A., & Sengupta, A. (2004). Risk factors for the development versus maintenance of posttraumatic stress disorder. *Journal of traumatic stress, 17*(2), 85-95. doi: doi:10.1023/B:JOTS.0000022614.21794.f4

Shalev, A. Y., Ankri, Y., Gilad, M., Israeli-Shalev, Y., Adessky, R., Qian, M., & Freedman, S. (2016). Long-term outcome of early interventions to prevent posttraumatic stress disorder. *The Journal of clinical psychiatry, 77*(5), e580-587.

Sharp, M.-L. (2019). Examining physical health conditions and associations of pain, obesity and function of UK veterans diagnosed with PTSD and other mental health diagnoses. *Journal of Military, Veteran and Family Health, 5*(2).

Sharp, M.-L., Fear, N. T., Rona, R. J., Wessely, S., Greenberg, N., Jones, N., & Goodwin, L. (2015). Stigma as a barrier to seeking health care among military personnel with mental health problems. *Epidemiologic reviews, 37*(1), 144-162.

Shay, J. (2014). Moral injury. *Psychoanalytic Psychology, 31*(2), 182.

Sippel, L. M., Holtzheimer, P. E., Friedman, M. J., & Schnurr, P. P. (2018). Defining Treatment-Resistant Posttraumatic Stress Disorder: A Framework for Future Research. *Biological psychiatry*.

Smith, S. M., Goldstein, R. B., & Grant, B. F. (2016). The association between post-traumatic stress disorder and lifetime DSM-5 psychiatric disorders among veterans: data from the National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III). *Journal of psychiatric research, 82*, 16-22.

Souza, W. F., Figueira, I., Mendlowicz, M. V., Volchan, E., Portella, C. M., Mendonça-de-Souza, A. C. F., & Coutinho, E. S. F. (2011). Posttraumatic stress disorder in peacekeepers: a meta-analysis. *The Journal of nervous and mental disease, 199*(5), 309-312.

Steenkamp, M. M., Litz, B. T., Hoge, C. W., & Marmar, C. R. (2015). Psychotherapy for military-related PTSD: a review of randomized clinical trials. *Jama, 314*(5), 489-500.

Stevelink, S. A., Jones, M., Hull, L., Pernet, D., MacCrimmon, S., Goodwin, L., . . . Greenberg, N. (2018). Mental health outcomes at the end of the British involvement in the Iraq and Afghanistan conflicts: a cohort study. *The British Journal of Psychiatry, 213*(6), 690-697.

Stirman, S. W., Finley, E. P., Shields, N., Cook, J., Haine-Schlagel, R., Burgess, J. F., . . . Gutner, C. A. (2017). Improving and sustaining delivery of CPT for PTSD in mental health systems: a cluster randomized trial. *Implementation Science, 12*(1), 32.

Sundin, J., Fear, N. T., Iversen, A., Rona, R. J., & Wessely, S. (2010). PTSD after deployment to Iraq: conflicting rates, conflicting claims. *Psychological medicine, 40*(3), 367-382.

Sundin, J., Herrell, R. K., Hoge, C. W., Fear, N. T., Adler, A. B., Greenberg, N., . . . Bliese, P. D. (2014). Mental health outcomes in US and UK military personnel returning from Iraq. *The British Journal of Psychiatry, 204*(3), 200-207.

The Management of Posttraumatic Stress Disorder Work Group. (2017). *VA/DOD Clinical practice guideline for the management of posttraumatic stress disorder and acute stress disorder*. Washington, DC.

Thompson, J. M., Pranger, T., Sweet, J., VanTil, L., McColl, M. A., Besemann, M., . . . Pedlar, D. (2015). Disability correlates in Canadian armed forces Regular Force veterans. *Disability and rehabilitation, 37*(10), 884-891.

Thompson, J. M., VanTil, L. D., Zamorski, M. A., Garber, B., Dursun, S., Fikretoglu, D., . . . Sudom, K. (2016). Mental health of Canadian Armed Forces Veterans: review of population studies. *Journal of Military, Veteran and Family Health, 2*(1), 70-86.

Van Hooff, M., Lawrence-Wood E, Hodson S, Sadler N, Benassi H, Hansen C, . . . AC, M. (2018). *Mental Health Prevalence, Mental Health and Wellbeing Transition Study*. Canberra.

Wang, H. E., Campbell-Sills, L., Kessler, R. C., Sun, X., Heeringa, S. G., Nock, M. K., . . . Stein, M. B. (2018). Pre-deployment insomnia is associated with post-

deployment post-traumatic stress disorder and suicidal ideation in US Army soldiers. *Sleep*.

Warner, C. H., Appenzeller, G. N., Parker, J. R., Warner, C. M., & Hoge, C. W. (2011). Effectiveness of mental health screening and coordination of in-theater care prior to deployment to Iraq: a cohort study. *American Journal of Psychiatry, 168*(4), 378-385.

Wessely, S. (2006). Twentieth-century theories on combat motivation and breakdown. *Journal of Contemporary History, 41*(2), 268-286.

Williamson, V., Stevelink, S. A., Greenberg, K., & Greenberg, N. (2018). Prevalence of mental health disorders in elderly US military veterans: a Meta-analysis and systematic review. *The American Journal of Geriatric Psychiatry, 26*(5), 534-545.

Williamson, V., Stevelink, S. A., & Greenberg, N. (2018). Occupational moral injury and mental health: systematic review and meta-analysis. *The British Journal of Psychiatry, 212*(6), 339-346.

Wilson, L. C. (2018). The prevalence of military sexual trauma: a meta-analysis. *Trauma, Violence, & Abuse, 19*(5), 584-597.

Wisco, B. E., Marx, B. P., Wolf, E. J., Miller, M. W., Southwick, S. M., & Pietrzak, R. H. (2014). Posttraumatic stress disorder in the US veteran population: results from the National Health and Resilience in Veterans Study. *Journal of Clinical Psychology, 75*(12), 1338-1346.

Wolf, E. J., Lunney, C. A., & Schnurr, P. P. (2016). The influence of the dissociative subtype of posttraumatic stress disorder on treatment efficacy in female veterans and active duty service members. *Journal of consulting and clinical psychology, 84*(1), 95.

Woodhead, C., Rona, R., Iversen, A., MacManus, D., Hotopf, M., Dean, K., . . . Jenkins, R. (2011). Mental health and health service use among post-national service veterans: results from the 2007 Adult Psychiatric Morbidity Survey of England. *Psychological medicine, 41*(2), 363-372.

Wright, B. K., Kelsall, H. L., Sim, M. R., Clarke, D. M., & Creamer, M. C. (2013). Support mechanisms and vulnerabilities in relation to PTSD in veterans of the Gulf War, Iraq War, and Afghanistan deployments: a systematic review. *Journal of traumatic stress, 26*(3), 310-318.

Xue, C., Ge, Y., Tang, B., Liu, Y., Kang, P., Wang, M., & Zhang, L. (2015). A meta-analysis of risk factors for combat-related PTSD among military personnel and veterans. *PloS one, 10*(3), e0120270.

Yehuda, R., Vermetten, E., McFarlane, A., & Lehrner, A. (2014). PTSD in the military: special considerations for understanding prevalence, pathophysiology and treatment following deployment. *European Journal of Psychotraumatology, 5*(1), 25322.