# At mission's end: the long-term impact of deployment on mental health

Wal, S.J. van der

# CHAPTER 7

## SUMMARY AND GENERAL INTRODUCTION

"*I have seen things that have changed me forever. I decided that I didn't want to look back. I didn't want to bother my loved ones and I pushed the people away who kept asking questions. I thought, if I work hard enough, I'll forget it."*[1]. From June till September 2007, veteran Erik worked as a military operating assistant in a NATO hospital in Kandahar, Afghanistan. Six years later, when Erik underwent surgery, it went wrong. *"That was a strong trigger. Suddenly I saw the operating room in Afghanistan"* In the weeks that followed, he got worse. Finally, he called the Veterans Institute. *"Asking for help was the hardest part for me. I had to admit I couldn't do it alone".* Within days, Erik received psychological help and was diagnosed with PTSD[1].

**Prevalence and trajectories of post-deployment mental health symptoms**

As the story of Erik shows, deployment-related mental health symptoms do not have to manifest immediately after trauma exposure. In the case of Erik, an event six years later reminded him of his time in Afghanistan and mentally returned him to the military hospital in Kandahar, which served as the trigger for the onset of his PTSD symptoms. However, posttraumatic stress can manifest at any time in a person's life. In the PRISMO cohort, a short-term PTSD symptom increase within the first six months after deployment was found. Six months post-deployment, 9% of the cohort indicated a high level of PTSD symptoms (probable PTSD prevalence). Besides this short-term effect, a long-term increase in symptoms five years after deployment was also revealed, with a probable PTSD prevalence of 13%[2]. In the present dissertation, a probable PTSD prevalence of 8% ten years after deployment was found (chapter 3). Although the prevalence of PTSD was still elevated compared to pre-deployment, it was a significant decline compared to five years post-deployment. This indicates that the subsequent increase in PTSD symptoms five years after deployment tapers off in the following years. Of course, this interesting finding is good news. But it also indicates that around 8% of the Dutch veterans who served in Afghanistan still suffer from substantial PTSD symptoms ten years after returning home. And that is a less optimistic message.

The risk of developing PTSD symptoms after homecoming from recent military missions has also been shown in several studies from different coalition partners (for a review, see:[3,4]). Longitudinal studies suggest a trend of stabilizing or aggravating PTSD prevalence rates[5,6]. Altogether, it underlines the importance of long-term monitoring of the mental health of deployed soldiers after a mission ends. Besides prevalence rates of PTSD, chapter 3 also shows the heterogeneity in symptom development among individuals. By using a latent growth mixture modeling technique, we identified four different trajectories of PTSD symptom development over the ten years after deployment: resilient (85%), improved (6%), severely elevated-recovering (2%), and delayed onset (7%). Although the majority of comparable studies had shorter follow-up

periods, the number and shape of these trajectories are very similar across studies[7-9], resulting in a solid scientific basis for the description of different trajectories of PTSD symptom development after deployment.

As the focus is often on veterans who struggle with post-deployment problems, it is worth highlighting that the large majority of deployed personnel, approximately 85% in the case of Dutch ISAF veterans, did not develop any PTSD symptoms in the ten years after deployment. Thus most service members deployed to war zones show enduring resilience despite exposure to traumatic stressors. Apart from individual risk- and protective factors, extensive military training and psychological preparation to handle all kinds of stressful situations that might be encountered during deployment will probably have contributed to the high degree of resiliency in Dutch military service members. Nevertheless, a considerable group (15%) did show symptomatic trajectories after homecoming. The individuals in the improved trajectory showed high symptoms pre-deployment and shortly after deployment, but gradual recovery after six months post-deployment. The individuals in the severely elevated-recovering trajectory had heavily increasing symptoms that showed recovery after five years post-deployment. Fortunately, the veterans in these trajectories show recovery after a period with moderate to severe PTSD symptoms. This does not apply to all veterans that showed PTSD symptoms. 7% of the veterans in our sample showed a delayed trajectory of increasing symptoms that reached the cut-off for PTSD between two and five years. Between five and ten years post-deployment, their symptoms were still increasing, although 77% of this group received some form of psychological care in the years after deployment. A decade after their deployments, we should especially be aware of this group of veterans.



Although other mental health symptoms beyond PTSD are more difficult to link to deployment directly, they can control the lives of veterans just as much and should therefore not be overlooked. In the present dissertation, we found that the probable prevalence of agoraphobia, anxiety, depression, and hostility symptoms significantly increased over time to respectively 7%, 3%, 4%, and 6% at ten years after deployment (chapter 4). Except for hostility symptoms, the probable prevalence at ten years after deployment was the highest compared to all previous follow-up measurements (although no probable prevalence is available at five years post-deployment). Up to two years post-deployment, the probable prevalence rates were quite low. Especially the increase in agoraphobia symptoms, from 3% at two years post-deployment to 7% at ten years post-deployment, is notable and a potential cause for concern. Based on large studies on aging and mental health symptoms in the general population[10,11], it can be suggested that the increase in mental health symptoms is related to deployment rather

than a result of the aging of the population. Therefore, these types of mental health symptoms may take longer to develop than PTSD symptoms within the aftermath of a significant stressful period such as a deployment. It is important to note that, despite this stressful period in their lives, as a group Dutch ISAF veterans still experience better mental health in terms of depression and anxiety compared to the general population. This seems plausible because we are dealing with a psychological healthy population pre-deployment that is psychologically tested before joining the army and extensively trained for military operations.

**Risk factors for post-deployment mental health symptoms**

Beyond the traumatic experience itself, individual vulnerability factors can contribute to developing mental health symptoms and developmental trajectories. Although military personnel are often seen by society as a very homogenous group of individuals that differ as a group from the general population, there is a lot of variation between service members in their childhood experiences, personality, military experience and social environment. Assessing which factors are related to increases in PTSD symptoms levels after deployment can help to identify who is most at risk. In chapter 3, we found that previously identified risk factors like younger age, lower rank, more deployment stressors, and less social support[2,6,12] were still relevant risk factors for the development of PTSD symptoms ten years after deployment. For the other mental health symptoms, we identified perceived social support from family and friends after returning home from deployment as the most important risk factor (chapter 4). Surprisingly, unit cohesion was not associated with any of the assessed mental health symptoms. Given that social support is potentially modifiable by providing intervention programs for military personnel and their family and friends, a wide range of mental health outcomes over a long period of time could be targeted in this way.

As targeted early interventions might especially be beneficial for veterans in the delayed onset PTSD trajectory to prevent worsening of their symptoms later in life, assessing risk factors for this trajectory might help identify these veterans when symptoms are still subclinical. We found that veterans in the delayed onset trajectory experienced a higher threat level during deployment and perceived less social support after returning home compared to veterans in the resilient group, but these risk factors also applied for the other symptomatic trajectories (chapter 3). Assessing differences in variables between individuals in the delayed onset group and individuals in the severely elevated-recovering trajectory would be highly informative to clarify why veterans in the latter trajectory were able to show a striking decline in PTSD symptoms between five and ten years after deployment as opposed to veterans in the delayed onset trajectory. However, no differences in the included variables were found. As a next step it would

be imperative to compare treatment history between these groups. In addition, recently identified biological mechanisms in the development and treatment of PTSD could be of considerable interest and may offer new perspectives.

One of these biological mechanisms of interest is DNA methylation. As epigenetic modification like DNA methylation reflects the complex interplay between environment and genes, it could be an underlying mechanism in the pathway from trauma to the development of mental health symptoms. In chapter 5, we studied longitudinal changes of DNA methylation profiles from pre-deployment to six months after deployment in relation to the development of PTSD symptoms up to five years after deployment. In line with previous research (for a review, see:[13,14]) we found evidence for associations between methylation changes and PTSD in our cohort. We identified four genetic regions with methylation changes over time that were significant determinants of the longitudinal development of PTSD symptoms. In addition, we also found initial evidence that post-deployment decreases in methylation at a genomic region in *EP300/miRNA1281* were also associated with the delayed onset trajectory compared to the resilient trajectory. This shows the potential of epigenetic marks to contribute to the successful identification of veterans with increased risk for developing delayed onset of PTSD in an early stadium where symptoms are still subclinical or even minimally present.

**Predicting PTSD development**

The identification of risk factors for PTSD, as also described in this dissertation, has not yet led to the development of effective pre-deployment screening tools or resilience-building initiatives[15]. It is common practice to study risk factors for PTSD by using traditional statistical methods. However, these methods are not able to capture non-linear and multidimensional relationships between predictors and the outcome of interest. Therefore, machine learning methods such as random forest modeling are increasingly implemented in psychiatric conditions to develop prognostic models[16]. In chapter 6, we trained a random forest model on pre-deployment variables, psychological as well as biological variables, to predict the development of PTSD symptoms up to ten years after deployment. The model performed well above chance (AUC = 0.71), and among the top five highest-ranked predicted features were self-reported symptoms (depression, anxiety and distrust and personal sensitivity) and biological markers (vasopressin and DEX-sensitivity). Some of the biological factors did not show significant associations with PTSD symptom development in the PRISMO cohort in previous studies that used linear mixed modeling, but were found to be important contributing variables in the present prediction modeling. This highlights the differences between machine learning and traditional statistical methods. As the

model performance on the current dataset was modest, the usability of the model as a ready-to-use pre-deployment screening tool is limited. However, the model offers important leads for the identification of risk factors for PTSD now that those factors have been analysed in conjunction, because as we know, factors never operate in isolation in something as complex as the development of a mental health disorder.

**A perspective on delayed onset PTSD**

When we speak about the impact of deployment on the mental health of service members, we usually do not look far ahead. We think about the problems that a veteran has to adapt to everyday life again, or about the prevalence rates of PTSD in the first few years after deployment. With this dissertation, I hope that I have convinced the reader to look beyond those first few years by showing the long-term impact that deployment can have on our service members. This long-term impact is represented by the identified group of approximately 7% of the Dutch ISAF veterans with a delayed onset PTSD. Ten years after their deployment, these veterans still suffer from increasing symptom levels. Health care professionals should be aware of this group of veterans with increasing treatment demands up to at least ten years after deployment, despite an average decline in symptoms in the population as a whole. However, the awareness of this group and its growing treatment needs alone does not seem to be enough. We know that even though the majority of this group seeks help, they do not seem to benefit from it. What are their perspectives in the current healthcare system? What needs to be changed to help them?

One theory for this group of veterans with a delayed onset of PTSD symptoms is that they might be a subpopulation of PTSD patients: a subpopulation with possibly different psychological and (neuro)biological underpinnings. Suggestions for distinct subtypes of PTSD have already been made on internalizing and externalization symptoms[17] and for a dissociative subtype[18,19]. Interestingly, the dissociative subtype which additionally suffered from depersonalization and derealization symptoms, was also distinguished by a delayed onset of symptoms. To date, only a few studies succeeded in characterizing PTSD subtypes in terms of biological correlates[20]. For example, the dissociative subtype was found to be related to altered subcortical white matter connectivity[21] and altered resting-state functional connectivity of the amygdala[22].

Biological and psychological correlates for delayed onset PTSD could be studied in a machine learning approach such as described in chapter 6, by comparing veterans with a delayed onset of PTSD symptoms to veterans with an early-onset of symptoms. The utilization of a machine learning approach for identifying military-related PTSD subtypes and their correlates has already been successfully demonstrated by Siegel and

colleagues[20]. In this study, two symptom severity PTSD subtypes were identified that could be distinguished by methylation, micro RNA and lactate markers[20]. Unfortunately, the sample sizes in the present study were too small to be able to make a comparison between a short-term and delayed onset of PTSD on the included risk factors. For future research, making this comparison could be an interesting starting point, as variation in psychological and (neuro)biological underpinnings may be a reason why veterans with a delayed onset of PTSD symptoms do not seem to respond adequately to available treatments[23].

Because we do not have a clear insight into the treatment history of veterans in the PRISMO study, it should first be sorted out whether treatment type and timing differ between veterans who show recovery between five and ten years after deployment (severely elevated-recovering) and veterans who do not show recovery in this period (delayed onset). There are several novel and interesting new perspectives on the treatment resistance of PTSD that are well worth exploring. In chapter 5, we demonstrated that changes in the DNA methylome were associated with the development of PTSD symptoms. However, there is also evidence that successful trauma-focused psychotherapy for PTSD restores these epigenetic marks[24]. Therefore it might be of interest to map and compare these methylation changes in veterans in a delayed onset trajectory and veterans in a severely elevated-recovering trajectory.

Another interesting perspective is that veterans with a delayed onset PTSD might suffer from another type of trauma. They might be exposed to traumatic events that violated their moral values, and therefore experience distress and functional impairments or 'moral injuries'[25,26]. Although it is still under debate whether veterans with underlying moral injury might or might not respond to evidence-based treatments for PTSD[26], novel treatment models that directly address moral injuries and their recovery might be more beneficial for veterans with a delayed onset of PTSD symptoms compared to the predominantly cognitive-behavioral based 'treatment-as-usual'. Another promising new approach that might demonstrate better efficiency in this group of veterans with suspected treatment resistance is using psychedelic drugs as adjuncts to facilitate psychotherapeutic treatments[27,28]. The treatment of sustained PTSD symptom severity might benefit from improvements in the capacity to engage with traumatic experiences in therapy induced by psychoactive substances[27,29]. This engagement in the processing of traumatic memories, for example in exposure-based therapies, might be particularly difficult for veterans with guilt and shame associated with the trauma. Integrating psychoactive substances within the psychotherapeutic treatment that specifically targets acts of commission, omission or betrayal[30] may address these challenges, and

could therefore catalyze the psychotherapeutic process and lead to better treatment outcomes in these veterans[27,31].

In addition to the hypothesis of possibly different psychological and biological underpinnings of their unresolved symptoms and the outlook for new treatment strategies for veterans in the delayed onset group, continued effort should be put into the identification and assessment of current PTSD symptoms in the veteran population. 23% of the veterans in the delayed onset group did not receive any psychological help in the ten years after deployment, although they experienced substantial levels of PTSD symptoms. In the face of the current monitoring policies that usually include routine screenings that stop after one or two years, there is still a lot to gain with more targeted and prolonged monitoring approaches.

**Ethical considerations of prediction models**

In the second part of this dissertation, I focused on the risk factors for post-deployment mental health symptoms and the development of a prediction model for long-term PTSD symptoms. The ultimate goal for this type of research is to develop a screening tool that can be used pre-deployment to get an accurate estimate of the PTSD risk for each service member that is listed to be deployed. For this purpose, service members will need to fill out specific questionnaires, blood would be taken, and a few neurocognitive tests would be taken. A trained algorithm would then evaluate this information, and after a few seconds, the commander in charge would know whether this service member will be deployed. This sounds like the newest episode of the Netflix-series *Black Mirror*, a scenario we don't see as realistic. Although there are a lot of remaining obstacles in the development of such a screening tool and error-free prediction will never be achieved, it is something we are working on in the research field. Of course, the goal of screening approaches to prevent PTSD development is noble and there are apparent positive consequences no one will debate. However, there are ethical implications of the pre-deployment identification of individuals that are at risk for developing PTSD after homecoming that should be discussed.

First, there is a risk of oversimplistic understanding and applications of predictive models for post-deployment PTSD symptoms[32,33]. As described in the fictional example above, it will be straightforward for the commander in charge to overvalue the model's classification output (PTSD: yes/no) by not taking the false positive and false negative rates into account. Algorithms for predictive models should therefore always be accompanied by clear information and education. But can we expect a user to fully understand a predictive model based on machine learning and to make an adequate assessment of the meaning and value of its outcomes? Especially in an

environment where so many interests play a role. And if we assume that the user is able to understand the model and its outcomes, how much should the presence of an increased risk for PTSD influence decisions about who can go to war or even who can stay in military service[32]? Will they simply exclude all candidates that screen positive? And how ethical is it if this decision is influenced by external factors like staff shortages? Are model outcomes suddenly assessed differently? Although prediction models for PTSD may protect some service members and their families from the psychological costs of mental health problems and the Ministry of Defence from long-term financial costs associated with mental health care and compensation claims, screening may lead to individual restrictions on someone's opportunity to be deployed based on an outcome that may not occur[32]. It therefore raises concerns of discrimination. Besides that, mandatory screening also raises questions about the confidentiality of highly privacy-sensitive data[34]. Are you obliged to provide this information to your employer? And if you do so, which persons within the military organization have access to your data?

If we take the perspective of the screened service member: what does it mean for an individual to know that you are at increased risk for developing PTSD after your deployment? First, it is almost impossible for a layperson to understand what the outcome of a classification model means. If you are not able to properly estimate the size of the risk, how can you then make the decision whether you should go on deployment or not? In addition, the knowledge that you are more vulnerable to develop mental health symptoms can negatively affect self-esteem and the relationships within a unit. One can imagine that it raises concerns in individuals about how they are perceived by their colleagues and commanders, or how it affects their military career. Merely the realisation that you are at increased risk could already lead to psychological problems. Furthermore, excluding service members with an increased risk for PTSD, whether it is on their own initiative or on the initiative of the organization, increases homogeneity within units and might even weaken them. For example, the identified risk factor 'distrust' that was incorporated in our predictive model, could also make an individual more alert to signs of danger and might thereby increase the safety of the unit in a warzone.

All these open questions and ethical concerns indicate that, as the development of predictive models for PTSD continues, a parallel and ongoing discussion on the moral implications is highly needed. Also, we should think about whether we want to invest in pre-deployment screening approaches or in the psychological support afterwards. A systematic review on pre-deployment psychological screening for disaster relief workers showed that, despite the attractiveness of screening for pre-deployment

indicators of resilience, the evidence base is very weak and does not support the use of pre-deployment screening as a method to protect the psychological health of disaster workers[35]. Of course, prediction models for PTSD are far from fully developed, and the inclusion of biological and neurocognitive measures can make a significant contribution to the predictive value of the models. But it is not inconceivable that these models will never be successful in preventing mental health problems. Investing in psychological support after homecoming from deployment, including appreciation and recognition which the Ministry of Defence is already strongly committed to, remains very important and worthwhile to keep improving.

**Limitations**

Although the PRISMO cohort enabled the differentiation of a range of vulnerability factors for the onset and long-term course of stress-related mental health problems in deployed military personnel and thereby makes an important contribution to the literature, the findings in the present dissertation should be interpreted in the context of its limitations. One of the most important limitations is the lack of a non-deployed military control group. For example, we are not able to compare the prevalence rates of mental health symptoms in our deployed cohort to the prevalence rates in a non-deployed control group. Therefore, it is not known whether the reported increase in symptom levels is exclusively the result of deployment. Furthermore, as frequently discussed in the previous chapters, we used self-report assessments of mental health symptoms which makes the results subject to the biases associated with the use of self-reports. Also, attrition is a significant concern and influence of non-response on the study results cannot be ruled out. However, we tried to minimize this effect by taking into account missing values in our analyses.

In the light of gender disparity in our scientific and medical knowledge base[36], there is a large underrepresentation of women in the PRISMO cohort. And although this is representative for the military, it is of high importance to study whether women respond differently to combat exposure. Also, deployment experiences may differ between men and women, as well as post-deployment factors like perception of family support or stigmatization. Due to the low percentage of women in the PRISMO cohort, we were not able to make comparisons between male and female veterans. Fortunately, research initiatives are emerging that specifically study the impact of deployment in military women (e.g.[37-39]). A final important limitation of the present dissertation is its focus on the individual. In the previous chapters we studied a range of risk factors for the development of mental health symptoms, but almost all of these factors relate to the individual. One important exception to this is social support. We identified decreased social support from family and friends after returning home from

deployment as one of the most important risk factors for developing mental health symptoms. It would therefore be of great interest for future research to elucidate the role of the partner, family and the military environment in the support system of veterans, and to investigate their influence on (preventing) development of mental health problems after homecoming.

## CONCLUDING REMARK

This dissertation falls within a large body of data and literature on the development of mental health problems after deployment. However, it is unique in the fact that it provides evidence for, and a description of, the long-term impact of deployment on service members up to ten years after deployment, with the ability to make comparisons to pre-deployment psychological health. With the ten-year measurement that formed the solid basis of this dissertation, the regular scheduled follow-up of the PRISMO cohort has come to an end. This does not mean that his cohort will not face difficulties in the future. Although it was not studied in the present dissertation, events later in life may serve as a trigger for the onset or worsening of mental health symptoms. Unfortunately, this concept has now painfully been tested by the recent events in Afghanistan. On August 15, 2021, the Taliban reached Kabul and the government crumbled. Afghanistan fell once again into the hands of the Taliban. As they watch the casualties inflicted on civilians, many Afghanistan veterans are feeling devastation and anger: *"It touches you because you've been there. You tried to change something. It looks like it didn't work out"*[40]. Significant events like the fall of Afghanistan bring back memories in many veterans that weren't present for a long time. As positive appraisals of service, or meaningful military engagement, might function as an aspect of psychological resilience[41], this event poses another substantial risk for the mental health of ISAF veterans. It teaches us that we must continue to commit ourselves to the psychological wellbeing of our veterans, even years after a mission's end. I hope this dissertation has contributed to that.

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