Using statistical techniques to understand the unique needs of military personnel experiencing mental health difficulties: moving away from assuming patient homogeneity to understanding heterogeneity

Laura Josephine Hendrikx [1,2], D Murphy [1,2]

ABSTRACT

Gold standard treatments for military personnel seeking support for mental health difficulties are often standardised and manualised to ensure high levels of treatment fidelity. While manualised treatments are preferable to less evidence-based idiosyncratic approaches, they may not fully account for the differences in symptom profiles present in patients with the same psychological diagnosis. Indeed, recent findings have highlighted that a significant proportion of individuals do not benefit from the 'gold standard' treatments. This brief report discusses the utility of statistical techniques, specifically latent profile analysis and network analysis, to support the transition to more evidence-based idiosyncratic, personalised care for clinical military, and general, populations. Further incorporation of such analysis methods may support arriving at a framework to support the personalisation of care in terms of the selection and adaption of evidence-based approach treatments based on individual clinical need.

Emerging evidence highlights that veterans are at increased risk of experiencing a range of mental health difficulties compared with their civilian counterparts and further that they have poorer treatment response to gold standard treatments. For example, a study of evidence-based treatment for military-related post-traumatic stress disorder (PTSD) demonstrated that 30%–61% did not attain clinically significant improvement and about 66% still met diagnosis at the end of treatment.[1] Clearly, there is a need to better understand how to support military personnel. One method that has been proposed is to move away from a 'one-size' fits all approach to treatment to personalising treatment based on the differing symptom profiles present within a diagnosis. The research underpinning widely used interventions rely on randomised controlled trials (RCTs) as 'gold standard' practice to evaluate their efficacy and effectiveness.[2] This has yielded plenty of evidence-based treatments for psychological disorders. For example, research supports the efficacy of trauma-focused cognitive behavioural therapy (TF-CBT) and eye movement desensitisation and reprocessing in treating PTSD.[3 4] However, there remains a lack of clarity as to *why* such interventions are effective. Furthermore, there remains concern over why a significant proportion of individuals do not respond to evidence-based, first-line treatments and/or experience a relapse of symptoms.[5 6]

Central to RCTs is an emphasis on using groups of participants, therapists and treatments that are as homogeneous as possible to minimise within-group variance and confounding factors. However, such an approach treats all patients diagnosed with the same disorder using the same treatments and does not account for within-group differences in symptom presentations. For example, researchers have concluded that there are over 600 000 combinations of symptoms that could result in a diagnosis of PTSD.[7] This may be particularly pertinent in military populations where data suggest a higher prevalence of avoidance symptoms (dissociation, emotional numbness, etc) as central to PTSD compared with re-experiencing symptoms (eg, flashbacks, nightmares, intrusive thoughts, etc).[8] Avoidance symptoms such as emotional numbness are not actively targeted by gold standard treatments that focus mainly on the re-experiencing symptoms.

The over-reliance on homogeneity within research has allowed us to arrive at evidence-based treatments that are effective for some but remain limited in meeting the varying needs of a significant proportion of individuals seeking support. While such subgroups have often been discussed as 'treatment-resistant', a likely more appropriate approach is to consider that interventions investigated under such homogeneous conditions may not be sufficient to meet individual needs across varying symptomatic presentations. As such, a switch of focus to the heterogeneity of clinical populations may be vital to enhancing psychological care. Observed rates of non-response and post-treatment relapse of symptoms has added to the tension between the reliance on manualised intervention versus more personalised, idiosyncratic care. Personalised approaches, also referred to as *precision medicine*, contrasts the medical model and 'aims to understand biological, genetic and environmental variation of diseases and to develop individually tailored treatments'.[9] Such an approach emphasises thorough assessment processes to develop an understanding and formulation of individuals' presenting difficulties and needs (ie, patterns of symptoms) and aims to deliver patient-focused interventions (ie, a personalised treatment plan).

The current debate between a focus on homogeneity and manualised treatment per diagnostic category versus heterogeneity and more idiosyncratic treatment may be reflective of a potential pending paradigm shift within the field of psychopathology. Alongside such discussions, there has been significant growth in available statistical methods supporting consideration of this switch. In this paper, we aim to discuss the utility of two statistical methods, namely, *latent profile analysis* (LPA) and *network analysis*, in the context of supporting the assessment of heterogeneity in psychological presentations and the evaluation of more personalised psychological treatment. These approaches allow researchers to compare military populations to other groups in order to derive a better understanding of potential differences in the symptom profiles. In turn, this can provide an evidence base to inform how to better personalise treatments for military populations. While this will be discussed in the paper within the context of PTSD and trauma-related difficulties, the implications are relevant to thinking of psychological disorders and distress more widely.

LATENT PROFILE ANALYSIS

LPA is a categorical latent variable modelling approach that can be used to identify subgroups within a population based on (a set of) certain variables.[10 11] Within

[1]Research Department, Combat Stress, Leatherhead, UK
[2]King's College London, London, UK

Correspondence to Ms Laura Josephine Hendrikx, Research Department, Combat Stress, Leatherhead, Surrey, UK; laura.hendrikx@kcl.ac.uk

psychopathology research, it can be used to determine how individuals group together in 'classes' or 'profiles' based on common symptom patterns. That is, each latent profile groups together those with similar experiences that differ from the experiences of those in another latent profile. As such, this allows research and clinicians assessing a group of patients to understand within-group differences that, in turn, could suggest how to tailor treatment. In practice, this may resemble 'triaging'; however, LPA offers the advantage for this triaging to be done based on different evidence-based symptom profiles rather than relying on clinical judgement alone. This is in line with findings that the symptomatic presentation of individuals with PTSD may greatly vary, and that PTSD often presents clinically with a range of comorbidities.[7 12] Take the example provided in Figure 1, where six different PTSD profiles were observed within a clinical sample of veterans.

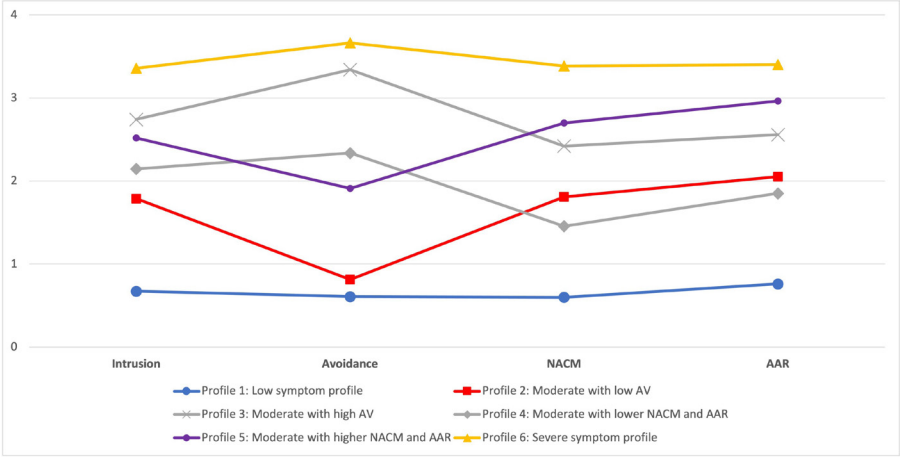

Figure 1 Example of latent class analysis.[5] AAR, alterations in arousal and reactivity; AV, avoidance; NACM, negative alterations in cognitions and mood.

At a population level, LPA can be used to better understand heterogeneity within populations by identifying more homogeneous subgroups based on presenting needs and difficulties. For example, an examination of the heterogeneity in PTSD presentations of Vietnam War veterans identified three subgroups, namely, those with no PTSD-related disturbance (61.4%; of which only 3% met PTSD criteria), moderate disturbance (25.6%; of which 34.2% met PTSD criteria) and those experiencing pervasive disturbance (12.5%; of which 87.6% met PTSD criteria).[13] Others have identified subgroup PTSD and complex PTSD (CPTSD) symptomatic presentations.[14] LPA can move further to the clinical level in highlighting relevant comorbidities and/or factors, such as certain experiences, associated with each latent profile. For example, Cloitre *et al* found that individuals with PTSD were more likely to have endured a single-event trauma, whereas those with CPTSD were more likely to have endured chronic trauma, as well as those with CPTSD were likely to experience greater functional impairment.[14] Another study found that veterans with an experience of killing were more likely to fit into a high PTSD symptomatology profile compared with intermediate, intermediate with low emotional numbing and low PTSD symptomatology profiles.[15] Moving down from the population to clinical level, LPA also offers insight into the symptom profiles within the subgroups including comorbidities and predicting or maintaining factors. Such understandings can support the idiosyncratic assessments of individuals seeking support for psychological disorders that may inform individual treatment plans developed through clinical expertise.

LPA holds additional benefits in the evaluation of treatment, specifically when looking at the predictors of treatment outcomes. That is, it may help understand some of the factors involved in higher non-response and symptom relapse rates within specific subgroups. An increasing number of studies have employed LPA and combined latent growth modelling approaches to better understand the variability in response to treatment.[5 16 17] For example, one study demonstrated that just about 30% of veterans who underwent psychological treatment demonstrated little change in PTSD severity ('treatment-resistance'), and that these veterans were more likely to have higher initial PTSD severity scores, comorbid depression and anxiety, and a previous combat role during their time in service.[5] Another study using a latent mixture modelling approach demonstrated that veterans with a low severity profile at intake (6.7%) responded positively to treatment whereas those with a high severity profile at intake primarily demonstrated small changes in symptom severity (32.5%) and only a small group demonstrated large positive changes (3.0%).[16] This study further showed that depression and guilt were likely to predict poor response to treatment.[16] The insight LPA offers in evaluating treatment outcomes in turn can highlight delivering more idiosyncratic assessments and treatment, for example, through the assessment of comorbid guilt and depression prior to PTSD treatment and adapting the trauma-focused intervention to first directly target depression and guilt cognitions.

NETWORK ANALYSIS

Network analysis is a novel statistical methodology that can be used to examine the connectivity between symptoms within a given psychological disorder, as well as with comorbid disorders or difficulties. Symptom network analysis steps away from the medical approach by conceptualising a mental health disorder (eg, PTSD) as a dynamic system of 'causally connected symptoms'.[18] That is, that symptoms and the interactions between symptoms *are* the disorder. Network analysis offers the opportunity to examine how likely it is that the activation of a given symptom will result in the activation of other symptoms in the network (ie, to determine the *centrality* of symptoms). This can provide information about which are most central (frequently occurring symptoms) in a presentation, allowing the application of interventions to target these central symptoms directly. Figure 2 provides an example of a network analysis of PTSD symptoms from a clinical sample of veterans (using a Diagnosis and Statistical Manual of Mental Disorders 5th edition (DSM-5) measure of PTSD). Within this network, 'recurrent thoughts' and 'a sense of detachment' were observed to be the most central symptoms. Clinically, gold standard treatments (such as TF-CBT) focus on the 'recurrent thoughts' symptoms but not the 'sense of detachment'. As such, results from this network analysis may suggest the importance of adapting interventions for veterans with PTSD to ensure they also target feelings of detachment and emotional numbing.

Implemented at the population level, network analysis can shed light onto the dynamic interactions between symptoms to understand key symptoms that work

to maintain the disorder, as well as how symptoms of the disorder may be casually associated with symptoms of comorbid difficulties. For example, a recent network analysis study exploring the relationship between PTSD and functional impairment suggested that changes in cognition and mood may be linked to functional difficulties in relationships, whereas PTSD reliving symptoms may be more strongly linked to functional difficulties in daily tasks such as home management.[8] Such findings suggest that specific symptoms may be targeted during intervention to relieve distress and break ties with comorbid difficulties. For example, equipping individuals with the tools to manage trauma reliving symptoms and associated emotional stress may help reduce the impact on daily functioning.

Network analysis resembles clinical case formulations that have long been used in the treatment of psychological disorders. Case formulations have been used as a way of generating clinically informed hypotheses of, for example, the interaction between predisposing, precipitating and perpetuating factors that contribute to an individual's psychological presentation. Case formulations rely on clinical expertise, whereas network analysis may provide a more robust evidence-based method to achieve similar results. Current discussion and emerging evidence suggest that single-case time-series networks (ie, intraindividual dynamic network analysis; IDNA) may offer a useful framework to understand the presentation and maintenance of disorders, as well as delivering personalised assessment and treatment.[19 20] IDNA can offer insight into how symptoms of given and/or comorbid disorder dynamically cluster together, which symptoms are most central within the dynamic network, which symptoms bridge different clusters of symptoms, and the strength of the dynamic interconnections between symptoms—*all at the individual level*.[20] Such an approach allows clinicians to develop a data-driven understanding of the key presenting difficulties that are relevant for clinical intervention for a given individual, as well as evaluate and support treatment outcomes through an understanding of how the network of symptoms change throughout treatment. IDNA remains a relatively new approach and there remain a minimal number of studies exploring its utility in practice.

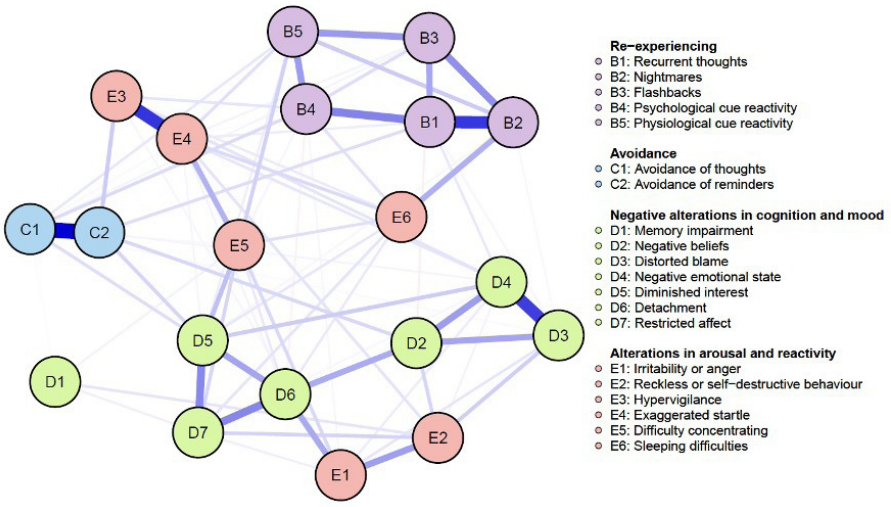

Figure 2 Example of network analysis: regularised partial correlation network of the 20 post-traumatic stress disorder symptoms in veterans: adapted from Ross *et al*.[8]

DISCUSSION

In this paper, we have discussed the advantages of statistical methods of LPA and network analysis to further understand the heterogeneity of mental health presentations within military population. Emerging evidence that veterans do not respond as well to current gold standard treatments highlights a clear need to understand how best to meet their needs. The application of such statistical methodologies at military population and clinical levels offers evidence-based methods to move away from a one-size fits all approach to treatment to adopting interventions more personalised to clinical needs of military personal.

Applied at the population level, LPA and network analytical approaches can shed light on the presentations of subgroups, for example, by identifying different symptom profiles present in individuals exposed to trauma and identify the best interventions for such differing presentations. Moving closer to the clinical level, these methodologies can aid clinicians in moving away from a one-size fits all treatment approach based on clinical diagnosis by providing an evidence-based approach to decide on the appropriate selection and/or tailoring of interventions to explicitly target the symptoms central to an individual's unique presentation. These approaches may support a shift to the provision of personalised care for military personnel, which may reduce the number of those who do not benefit from current gold standard treatments. With such statistical advances offering the opportunity to focus on heterogeneity, further research can be conducted to trial delivering psychological treatment in a way that matches specific treatment components or modules with specific needs. As most of the research on evidence-based interventions have often not focused on identifying the mechanisms of action (ie, why the interventions work), such future research may help identify what treatment components match with certain symptomatic profiles. It may also be necessary for further work to develop new interventions that align with presenting difficulties. For example, more modular approaches may allow delivering treatment modules based on the presenting need and difficulty of the individual seeking support.[21]

Switching focus to more personalised care holds clear clinical implications in that evidence-based interventions can be selected and delivered according to the needs of the individual seeking support. Assumingly, this may enhance treatment outcomes in terms of reducing non-response and relapse of symptoms, and ideally promote client engagement through better alignment of interventions and experiential distress. However, investigation of the feasibility and effectiveness of such approaches is required. Finally, switching to more personalised care may hold important societal gains. The reliance on manualised, one-sized-fits-all approach has historically been argued to be cost-effective, especially within the context of limited resource. However, given the significant proportion of those who do not respond to treatment (in particular, with military populations), have recurrent engagement with services and the functional impairment that may occur over such periods, more personalised approaches may prove to be more cost and resource effective in the long term. This move towards personalised care is not intended to cross out the delivery of existing evidence-based treatments, as they have over time proven to be effective

in supporting a significant number of individuals experiencing psychological distress. On the contrary, personalised care will allow the recognition of where such treatments may be effectively delivered as well as deliver adapted treatments where there is clinical rationale to do so.

Contributors Both authors completed to the writing and revision of the current manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Hendrikx LJ, Murphy D. *BMJ Mil Health* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/military-2022-002253

Received 14 November 2022
Accepted 20 January 2023

BMJ Mil Health 2023;**0**:1–4.
doi:10.1136/military-2022-002253

ORCID iDs
Laura Josephine Hendrikx http://orcid.org/0000-0001-6760-3373
D Murphy http://orcid.org/0000-0002-9530-2743

REFERENCES

1 Steenkamp MM, Litz BT, Hoge CW, *et al*. Psychotherapy for military-related PTSD: a review of randomized clinical trials. *JAMA* 2015;314:489–500.
2 Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N Engl J Med* 2000;342:1887–92.
3 Bisson JI, Ehlers A, Matthews R, *et al*. Psychological treatments for chronic post-traumatic stress disorder. systematic review and meta-analysis. *Br J Psychiatry* 2007;190:97–104.
4 Bradley R, Greene J, Russ E, *et al*. A multidimensional meta-analysis of psychotherapy for PTSD. *Am J Psychiatry* 2005;162:214–27.
5 Murphy D, Smith KV. Treatment efficacy for veterans with posttraumatic stress disorder: latent class trajectories of treatment response and their predictors. *J Trauma Stress* 2018;31:753–63.
6 Steinert C, Kruse J, Leichsenring F. Long-term outcome and non-response in psychotherapy: are we short-sighted. *Psychother Psychosom* 2016;85:235–7.
7 Galatzer-Levy IR, Bryant RA. 636,120 ways to have posttraumatic stress disorder. *Perspect Psychol Sci* 2013;8:651–62.
8 Ross J, Murphy D, Armour C. A network analysis of DSM-5 posttraumatic stress disorder and functional impairment in UK treatment-seeking veterans. *J Anxiety Disord* 2018;57:7–15.
9 Silberschatz G. Improving the yield of psychotherapy research. *Psychother Res* 2017;27:1–13.
10 Howard MC, Hoffman ME. Variable-centered, person-centered, and person-specific approaches. *Organizational Research Methods* 2018;21:846–76.
11 Spurk D, Hirschi A, Wang M, *et al*. Latent profile analysis: a review and "how to" guide of its application within vocational behavior research. *Journal of Vocational Behavior* 2020;120:103445.
12 Ginzburg K, Ein-Dor T, Solomon Z. Comorbidity of posttraumatic stress disorder, anxiety and depression: a 20-year longitudinal study of war veterans. *J Affect Disord* 2010;123:249–57.
13 Steenkamp MM, Nickerson A, Maguen S, *et al*. Latent classes of PTSD symptoms in vietnam veterans. *Behav Modif* 2012;36:857–74.
14 Cloitre M, Garvert DW, Brewin CR, *et al*. Evidence for proposed ICD-11 PTSD and complex PTSD: a latent profile analysis. *Eur J Psychotraumatol* 2013;4:20706.
15 Maguen S, Madden E, Bosch J, *et al*. Killing and latent classes of PTSD symptoms in iraq and afghanistan veterans. *J Affect Disord* 2013;145:344–8.
16 Phelps AJ, Steel Z, Metcalf O, *et al*. Key patterns and predictors of response to treatment for military veterans with post-traumatic stress disorder: a growth mixture modelling approach. *Psychol Med* 2018;48:95–103.
17 Schumm JA, Walter KH, Chard KM. Latent class differences explain variability in PTSD symptom changes during cognitive processing therapy for veterans. *Psychological Trauma: Theory, Research, Practice, and Policy* 2013;5:536–44.
18 Borsboom D, Cramer AOJ. Network analysis: an integrative approach to the structure of psychopathology. *Annu Rev Clin Psychol* 2013;9:91–121.
19 David SJ, Marshall AJ, Evanovich EK, *et al*. Intraindividual dynamic network analysis - implications for clinical assessment. *J Psychopathol Behav Assess* 2018;40:235–48.
20 Epskamp S, van Borkulo CD, van der Veen DC, *et al*. Personalized network modeling in psychopathology: the importance of contemporaneous and temporal connections. *Clin Psychol Sci* 2018;6:416–27.
21 Karatzias T, Cloitre M. Treating adults with complex posttraumatic stress disorder using a modular approach to treatment: rationale, evidence, and directions for future research. *J Trauma Stress* 2019;32:870–6.