Bipolar Audit Evidence Synthesis

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MELBOURNE

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Acknowledgements of Country

In the spirit of reconciliation, Phoenix Australia acknowledges the Traditional Custodians of country throughout Australia and their connections to land, sea, and community. We pay our respect to their Elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples.

Disclaimer

The views and recommendations stated in this report are solely those of Phoenix Australia and do not reflect those of the Department of Defence or the Australian Government.

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Contents

This report has been formatted to provide the results of the evidence synthesis first, with the detailed background, methodology and evidence synthesis presented following.

This report has five key sections:

(1) Summary of results and key findings from the evidence synthesis,
(2) Background information,
(3) Overview of the literature pertaining to the general population,
(4) Our systematic search methodology conducted on the military literature and,
(5) Results of the systematic search.

Previous research has found higher prevalence of bipolar disorder (BD) among current (2.8%) and ex-serving (9.8%) Australian Defence Force (ADF) members compared to the civilian communities (0.9 – 1.7%) and other military samples (McFarlane et al., 2011; Van Hooff et al., 2018). However, a recent audit of the Defence Electronic Health System Records found extremely low rates of BD among current serving members (0.03%). This disparity could be due to a number of reasons, including low levels of BD among current serving members, under-diagnosis, delayed onset of characterising symptoms, low levels of treatment seeking, or potential misdiagnosis of BD for other disorders (Cerimele et al., 2017, 2020; McLay et al., 2014).

To achieve greater understanding of BD key risk factors, differential diagnosis, evidence for screening tools, and best practice clinical management, a systematic literature search was undertaken with the aim of reviewing existing evidence. In addition, an expert panel of military psychiatrists was consulted, including engagement with the international Five Eyes consortium of researchers.

1 Key findings from the evidence synthesis

The primary risk factors for BD relevant to screening in the military include:

- **Family history**
- **Childhood trauma**
- **Psychological stress**
- **Substance use**
- **Deployment**

In the case of differential diagnosis, **BD is most commonly misdiagnosed as depression** due to patients often first presenting with depressive symptoms (O'Donovan & Alda, 2020). Up to 40% of patients with BD will receive an inaccurate diagnosis, often MDD (Stiles et al., 2018), as individuals will typically transition from MDD to BD and then symptoms are not reassessed. **BD is also found to share several clinical features with PTSD, and personality disorders** Emotionally Unstable Personality Disorder and Narcissistic Personality Disorder. BD is found to co-occur with other disorders such as Attention-deficit/Hyperactivity Disorder (ADHD), and the panel of experts consulted for this project recognised the **challenge of distinguishing adult ADHD from hypomania**. The Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition has undergone several revisions which saw substantial amendments to BD diagnostic criteria compared to the DSM-IV. New criteria may contribute to diagnostic delay. There was consensus

between the literature and the expert panel recognising the disadvantages of self-report measures, highlighting the necessity for clinician interview to determine diagnosis. Moreover, the experts recommend frontline clinicians should be better trained in the detection and management of the disorder.

Similarly, the Royal Australian and New Zealand College of Psychiatrists (RANZCP) clinical practice guidelines for mood disorders highlight the **importance of a clinical interview for the diagnosis of BD**, which should include considering risk factors, comorbidities, prodromes, and potentially triggering life events. During treatment for BD, the guidelines recommend not to focus solely upon acute management but also preventative treatment and ongoing maintenance, in addition to stressing the importance of a multidisciplinary network of providers for the successful management of the disorder. Further, both pharmacotherapy and psychological intervention are recommended.

At this point in time, evidence specific to BD key risk factors, differential diagnosis, screening tools, and best practice management in military members is lacking, however, guidance can be taken from research in civilian populations.

2 Background

Bipolar Disorder (BD) is a chronic affective disorder characterised by recurrent depressive and manic episodes (Carvalho et al., 2020). Frequency of mood fluctuations can be rapid cycling (four or more mood episodes in a 12 month period) and days or weeks, or may last longer periods of time and be separated by several years (Gordovez & McMahon, 2020). Symptoms of the disorder typically begin to present between the ages of 18 and 24 (Gordovez & McMahon, 2020), with some evidence suggesting the disorder is more common among men than women (Miller & Black, 2020). Moreover, prevalence of medical and psychiatric comorbidities is high (Grande et al., 2016).

The 2010 Australian Defence Force (ADF) Mental Health Prevalence and Wellbeing Study Report and the 2018 Mental Health Prevalence, Mental Health and Wellbeing Study found higher prevalence of BD among current (2.8%) and ex-serving (9.8%) ADF members compared to the civilian communities (0.9 – 1.7%) (McFarlane et al., 2011; Van Hooff et al., 2018). These studies also found higher rates of Posttraumatic Stress Disorder (PTSD) when compared with the Australian civilian population. Comparably, the Joint Health Command *Bipolar and Post-traumatic Stress Disorders in the ADF: Estimating Prevalence from Defence Electronic Health System Records* found an extremely low prevalence of BD (0.03%) and PTSD (0.96%). These low rates of detection highlight the possibility of under-diagnosis, low levels of treatment seeking for these symptom presentations, and/or delayed onset.

The issue of possible under-diagnosis of BD may be related to a range of factors, including a lack of education and training among military healthcare providers, and no systematic screening for mania symptoms (the identifying feature of BD). Furthermore, within military populations internationally, it has been identified that BD is often under-diagnosed, and there are particular challenges in diagnosis due to the some symptom overlap with PTSD (McLay et al., 2014), as well as some characteristic symptoms of mania potentially not being identified as problematic within the military, particularly within the deployment context (Cerimele et al., 2017, 2020).

A large US study of the progression of subthreshold BD to diagnosed disorder over time found that there were a number of hypomania symptoms present at subthreshold levels early in symptom trajectory that were associated with particular risk: decreased need for sleep, unusually high energy, and increased goal-directed activity (Bach et al., 2021; Rabelo-da-Ponte et al., 2020). The relative non-specificity of symptoms such as these, combined with their advantageous benefits in the context of military service, make it likely that these behaviours may not be identified as signs of risk in routine screening. There is also broader evidence from community studies that milder forms of BD are often missed in clinical practice in general (Carvalho et al., 2015), with diagnosis of BD taking up to 10 years from initial onset of affective symptoms (Dagani et al., 2017; Drancourt et al., 2013; Lish et al., 1994).

There is some evidence that PTSD may predict the development of both major depressive disorder and BD in civilian populations (Chou et al., 2014; Goldstein & Levitt, 2007; Jacobson & Newman, 2017), and there is some comorbidity between these disorders in both civilian and military populations (McLay et al., 2014; Nichter et al., 2020; Reddy et al., 2017). Thus, the issue of detection of subthreshold presentations for both BD and PTSD, particularly in the presence of depressive symptoms is of importance. However, detection of BD and differential diagnosis can be challenging.

A number of recent studies have started to address the issue of BD detection and differential diagnosis within military and veteran samples (Cerimele et al., 2017, 2020; Cogan et al., 2021), with promising findings. For example, a recent study examining screening tools for BD and depression (Cerimele et al., 2022) suggests the combination of brief depressive and mania screens may be of significant utility in detecting early hypomanic symptom presentations, which warrant further investigation or monitoring.

The following section will include a review of the literature pertaining to the general population, followed by the systematic search outcomes and literature relevant to military populations.

3 General population overview

Risk factors

Summary of risk factors - clinical staging model

1. At-risk

- presence of Major Depressive Disorder (MDD)
- first or second degree relative
- *MDD + family history of BD = ultra-high risk*

2. Potential prodromal

- mood disorder symptoms
- subthreshold mania or hypomania
- sleep issues (e.g., longer sleep duration, increased sleep latency)
- change from usual behaviour
- affective liability
- dissociative symptoms
- excessive energy or talkativeness
- hyperactive behaviour
- overly productive goal directed behaviour
- reckless behaviour
- racing thoughts
- lack of energy
- decreased functioning
- feelings of worthlessness
- suicidal thoughts

Other proposed risk factors

- ADHD
- younger age of depression onset
- use of mood stabilisers and antidepressants
- recurrent depression
- psychotic symptoms in the presence of depression
- admission to hospital with depression
- poorer global functioning within individuals with depression and family history of BD

Early diagnosis is crucial for improving outcomes for people with BD. Unfortunately, delayed diagnosis is not uncommon for BD, with a 10-year average delay for diagnosis of the disorder (Baldessarini et al., 2006). Growing knowledge of the aetiology of BD has helped to distinguish early risk factors and enhance capability of identifying at-risk individuals (Álvarez-Cadenas et al., 2023). The International Society for Bipolar Disorders (ISBD) Task Force – a team of international experts – have endorsed a clinical staging model for BD to improve risk identification through risk profiling (Kupka et al., 2021). This clinical staging model proposes that individuals can be placed on an illness trajectory based on their degree of risk, prodromes, or

disorder symptoms which may allow for targeted, stage appropriate early-intervention or treatment, however further research is necessary to confirm the clinical utility of the model (Kupka et al., 2021).

Whilst several, yet similar, clinical staging models for BD exist, all BD-specific models concur that trajectories begin at an 'at-risk' phase (Kapczinski et al., 2014). This latent stage identifies individuals who are at greater risk for BD but are asymptomatic (Kapczinski et al., 2014). The most well understood latent indicator of risk is confirmed presence of Major Depressive Disorder (MDD) or BD in a first- or second-degree relative (Kupka et al., 2021; McCarthy et al., 2022). A complex interplay between genetic and environmental factors is considered to underly BD heritability, however the exact interaction is not yet well understood (O'Connell & Coombes, 2021).

The Task Force have emphasised that detection of prodromes, that is, a change from usual behaviour and experiences prior to meeting criteria for disorder, is essential for predicting disease onset and improving prognosis (Álvarez-Cadenas et al., 2023). The next stage within the clinical staging model of BD proposes that individuals presenting with prodromes, such as mood disorder symptoms, indicate further risk for BD. Subthreshold mania or hypomania lie further along the trajectory and are at greater risk for illness progression (Kupka et al., 2021; McCarthy et al., 2022). Individuals meeting criteria for MDD who have a family history of BD are at ultra-high risk for BD (Kupka et al., 2021).

Notably, circadian rhythm abnormalities and changes in sleep are often present among individuals at-risk for BD (Leopold et al., 2012; McCarthy et al., 2022). Chronotype, referring to the synchronisation between the external environment and sleep cycle, is one proxy measure of circadian rhythm which has been implicated in BD and may have genetic underpinnings (Zou et al., 2022). Other sleep disruptions, such as higher sleep duration and increased sleep latency, are also associated with BD, particularly during depressive episodes (Panchal et al., 2022).

Further prodromes which indicate BD risk include anxiety or fearfulness, affective lability, symptoms of dissociation (Leopold et al., 2012), excessive energy and talkativeness, hyperactive behaviour, overly productive goal-directed behaviour (Álvarez-Cadenas et al., 2023), reckless behaviour, racing thoughts, lack of energy, decreased functioning, feelings of worthlessness, and suicidal thoughts (Andrade-González et al., 2020). Moreover, 10-12% of patients with ADHD will develop BD, demonstrating that ADHD may be an indicator of greater risk (Brancati et al., 2021). Factors associated with transition from MDD to BD include younger age of onset, use of mood stabilisers, recurrent depression, psychotic symptoms, and admission to hospital psychiatric ward (Kim et al., 2020). For individuals with family history of BD, poorer global functioning prior to the onset of prodromes indicated greater likelihood of transition to BD (Watson et al., 2023).

Misdiagnosis

Clinical presentation

Later stages of the clinical staging model are marked by BD symptoms and indicate likelihood of remission according to symptomology, with the end of the trajectory comprising BD with poor prognosis (Kupka et al., 2021). Lack of identification of BD prodromes or misidentification of BD symptoms in these later stages can have negative implications through lack of early intervention or treatment, resulting in progression along the

trajectory and poorer prognosis (Wang et al., 2020). Up to 40% of patients with BD will receive an inaccurate diagnosis, often for MDD (Stiles et al., 2018), as patients present during a depressive mood episode. Specifically, melancholic or psychotic depression indicate greater likelihood of BD (Parker, 2016), and if either are present, a careful assessment for BD is necessary. Melancholic depression is a severe subtype of MDD characterised by persistently low mood, anhedonia, psychomotor disturbance, cognitive impairment, and insomnia (Gili et al., 2012), whereas psychotic depression involves psychotic features such as delusions or hallucinations (Wijkstra et al., 2013). It is also worth noting that the diagnosis of a depressive episode or MDD may be accurate at the time due to no reported previous symptom elevation.

Existing literature demonstrates strong consensus that depression with an early onset or recurrent course, subthreshold hypomanic or mixed symptoms, and family history of BD or completed suicide likely indicates that BD is present or will emerge and should be carefully considered by clinicians (O'Donovan & Alda, 2020). Further, BD often co-occurs with other psychiatric disorders and, combined with the considerable symptom overlap, increases likelihood of misdiagnosis (Brancati et al., 2021). BD and ADHD often co-occur and display overlap in symptomology such as hyperactivity and excessive energy, leading to frequent inaccurate diagnoses, particularly in childhood and adolescence (Álvarez-Cadenas et al., 2023; Brancati et al., 2021). Borderline Personality Disorder (BPD) and Narcissistic Personality Disorder also share some of the clinical features of BD, such as mood dysregulation and grandiosity, respectively (Malhi et al., 2021; Nagel et al., 2022). A key differentiation between BD and BPD is the sustained mood episodes in BD, compared to fluctuating mood in BPD (Malhi et al., 2021). PTSD symptoms also overlap with BD symptoms, particularly among military personnel returning from war deployments. Several features, such as poor sleep and concentration, irritability, and reckless behaviour are common after war experiences and these symptoms can manifest as either PTSD or hypomania (Brennan & Tanev, 2018). However, this differentiation is important for optimal treatment response, with a recent systematic review concluding comorbid PTSD in those with BD may affect the response of quetiapine and lithium (Russell et al., 2023).

Diagnostic tools

With the aim to enhance precision of diagnostic criteria and prevent inaccurate diagnoses, an expert taskforce was created and alternative criteria to the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition were generated (Parker et al., 2022). Changes included: 1) removal of impairment as a necessary criterion; 2) removal of hospitalisation as automatic assignment to a particular BD subtype; 3) adding symptoms of anger and irritability; 4) removal of a mandatory duration for hypomania or mania; and 5) a greater number of symptoms being necessary for diagnosis. New criteria trialled were shown to distinguish BD from unipolar depression (Parker et al., 2022). Studies have shown lower prevalence of BD diagnosis using diagnostic criteria in the DSM-5 and International Classification of Diseases (ICD) 11th edition when compared to the previous DSM-IV and ICD-10 (Kessing et al., 2021). From this, researchers have concluded that DSM-5 and ICD-11 criterion will result in diagnostic delay (Kessing et al., 2021). In addition to these tools, the interviewer-administered Composite International Diagnostic Interview (CIDI) has been widely used for BD, particularly in prevalence studies, however it is worth noting that depending on the algorithm used, overdiagnosis can occur (Mitchell et al., 2013).

Screening tools

According to the clinical staging model, transition to BD occurs when an individual progressing along the trajectory from the 'at-risk' or prodromal stage and reaches the syndrome stage, beginning either with symptoms of mood disorder or hypomania/mania (Kupka et al., 2021). Indeed, selecting the right screening method is vital for prevention of misdiagnoses (Culpepper, 2014). The Hypomania Checklist (HCL-32) and the Mood Disorder Questionnaire (MDQ) have been developed to diagnose BD and differentiate from MDD. The HCL-32 and MDQ are two of the most widely used instruments and have been shown to have similar sensitivity for differentiating BD from MDD (Wang et al., 2019). However, the HCL-32 and MDQ do not demonstrate precision diagnostic capacity and should be supported by clinical interview to improve accurate diagnoses (Baek et al., 2020; Zimmerman, 2022). The MDQ and HCL-32 have also been shown to demonstrate false positive diagnoses by picking up on trait impulsivity and increased anxiety (Baek et al., 2020). Clinical interview is important for evaluating degree of BD risk, prodromes, or symptom characteristics. Through clinical interview, thorough consideration may be given to family history, environmental factors, co-occurring psychiatric disorders, and detailed insight into symptom onset, frequency and severity (Culpepper, 2014).

In considering the clinical staging model for BD, it is apparent that the early identification of prodromal symptoms is more favourable than identifying BD when it reaches disorder level. A recent review by Álvarez-Cadenas et al. (2023) found that clinical interview was the most common method for identifying BD prodromes. A mixture of structured and ad-hoc interviews were employed to identify prodromes, with a variety of instruments being utilised within clinical interviews, including questionnaires, symptom checklists and scales (Álvarez-Cadenas et al., 2023). One measure was shown to be the most widely used, valid and reliable measure for prodromal symptoms among adults, which was the Bipolar Prodrome Symptom Interview and Scale-Prospective (BPSS-P) administered via semi-structured interview (Álvarez-Cadenas et al., 2023).

In more recent years the role of technology, including wearables, has been trialled for utility in diagnosis and the monitoring of BD symptoms (Antosik-Wójcińska et al., 2020; Dunster et al., 2021; Saccaro et al., 2021). Further, researchers have reported testing machine learning algorithms and models in an effort to predict the disorder. While smartphone monitoring tools and machine learning have shown some success in the diagnosis of BD (Dunster et al., 2021; Jan et al., 2021), accuracy remains variable and additional research is necessary prior to adopting newer technologies and methods.

Best Practice Clinical management

In 2020, the Royal Australian and New Zealand College of Psychiatrists (RANZCP) released clinical practice guidelines for mood disorders, including for the management of BD (Malhi et al., 2021). This document provides a succinct and useful summary of diagnosis and classification, assessment and formulation, and treatment principles.

There are several factors to consider when assessing BD diagnosis, including the period of depression prior to mania (typically occurring in adolescence), family history, confounding personality factors (especially when there is affective instability), and comorbid substance misuse obscuring symptoms. It is recommended that assessment includes understanding the course of illness, which assists in determining patterns including

duration of depression and mania, and elucidates whether presentation includes predominantly depression, mania, or mixed states. Further, it is important to note triggering life events, including but not limited to antidepressant-induced elevated states (O'Donovan & Alda, 2020).

In terms of treatment, it is important not to focus solely upon acute management but also preventative treatment and ongoing maintenance. The 2020 RANZCP clinical practice guidelines for mood disorders note the importance of a multidisciplinary network of providers for the successful management of BD, led by a psychiatrist or primary care physician. For best practice treatment of BD, both pharmacotherapy and psychological intervention are recommended. The RANZCP guidelines note four evidence-based therapeutic approaches: Psychoeducation, Cognitive-Behavioural Therapy (CBT), Family focused Therapy (FFT) and Interpersonal and Social Rhythm Therapy (IPSRT), which all share active collaboration and a skill-development focus (Malhi et al., 2021).

The RANZCP guidelines propose a framework including three key elements for the best practice management of BD: *Actions, Choices, Alternatives*, which should be applied to each phase of the illness. *Actions* include those that can be implemented by the patient (e.g., regular exercise, healthy diet), and those implemented by primary care physicians or therapists (e.g., psychoeducation, therapeutic and pharmacologic intervention). Actions may also include enhancing social support, addressing issues such as housing or employment, and addressing maladaptive habits (e.g., substance misuse) with the assistance from specialists. The *Choices* element of the framework includes pharmacological options across phases of the disorder, while the *Alternatives* element includes additional strategies not already covered within Choices (e.g., ECT). These recommendations, including specific pharmacological agents, are thoroughly detailed in the RANZCP guidelines (see Malhi et al. (2021)).

Importantly, as described in the Screening section, clinical interview is considered the most valid method to diagnose BD (Zimmerman, 2021). The evaluation of BD symptoms requires clinical expertise, careful review, and consideration of the course of symptoms to determine acute phases and stability. In summary, for best practice management of BD, the RANZCP guidelines describe the requirement for sophisticated pharmacotherapy for both acute phases and long-term maintenance of the disorder, in addition to adjunct psychological intervention, and management as guided by the Actions, Choices, Alternatives framework.

In order to support primary healthcare providers to appropriately identify BD within military populations, there is the need for the development of military-specific evidence-informed education and training materials. To date, limited research exists regarding BD presentations and diagnosis within military populations, including subthreshold presentations, which may not be associated with functional impairments within this occupational context. However, there is a concerted effort within the research community to address this, with a significant number of studies emerging in recent years. The following section of the report details research relevant to BD as per the aforementioned categories (risk factors, misdiagnosis, screening tools, and best practice), specific to the military.

4 Military evidence review

Aim

The aim of the current evidence report is to review existing evidence and provide brief overview of the (a) risk factors for BD; (b) differential diagnosis (including BD/PTSD comorbidity) and screening tools; and (c) best practice clinical management of the disorder.

Method

A systematic literature search was undertaken to gather recent evidence relevant to risk factors for BD; differential diagnosis (including BD/PTSD comorbidity and other affective disorders), screening tools, and best practice clinical management for military populations. A protocol was developed which included the Patient, Intervention, Comparator, and Outcome (PICO) strategy (see Table 1).

Population	Active serving military personnel
Intervention	N/A
Comparator	N/A
Outcome	Diagnosis, clinical management, screening, risk factors

Table 1. Search strategy PICO

The intervention and Comparator components of the PICO were not relevant to the current search strategy and thus, the PO (Population and Outcome) were used to define parameters for the systematic search.

Search strategy

EMBASE, MEDLINE and PsycINFO were searched for human studies published between 2012 – current in English language. Search terms were specific to military; diagnosis, screening or risk; BD; or PTSD comorbidity and were limited to abstract(s), title(s), and keyword(s) (see Table 2).

Keyword:	**Combined with:**
Military	*OR*
ADF	*OR*
Defence	*OR*
Special operation*	*OR*
Special force*	*OR*
Armed force*	*OR*
Navy	*OR*
Army	*OR*
Airforce	*OR*
Air force	*OR*

Troop*	*OR*
National guard*	
AND	
Diagnos*	*OR*
Identif*	*OR*
Risk*	*OR*
Screen*	
AND	
Bipolar	*OR*
Bi-polar	
OR	
Comorbid*	*AND*
PTSD	*OR*
Post traumatic stress disorder	*OR*
Posttraumatic stress disorder	*OR*
Post-traumatic stress disorder	

Table 2. Keywords used in systematic search

Inclusion and exclusion criteria

Randomised controlled trials, quasi-randomised controlled trials, cohort studies or other observational studies, reviews, editorials or commentaries, and case studies including adult humans (>18 years) were included. Articles were included if they assessed BD risk factors, comorbidity, diagnosis, screening tools, clinical management, or comorbidities in active military personnel. Studies of adults with or without diagnosed BD were included. Articles were excluded if they assessed BD treatment response, or their sample population was children, adolescents, or non-military cohorts.

Screening and selection was completed using the systematic record management tool Covidence Systematic Review Software (Covidence, 2021). Abstracts were screened by one reviewer (KM) and relevant articles were progressed to the full-text review stage. Records which progressed to full-text review were examined by two reviewers (KM and AS) against inclusion and exclusion criteria and conflicts were resolved by discussion. Reasons for exclusion were documented (see Figure 1).

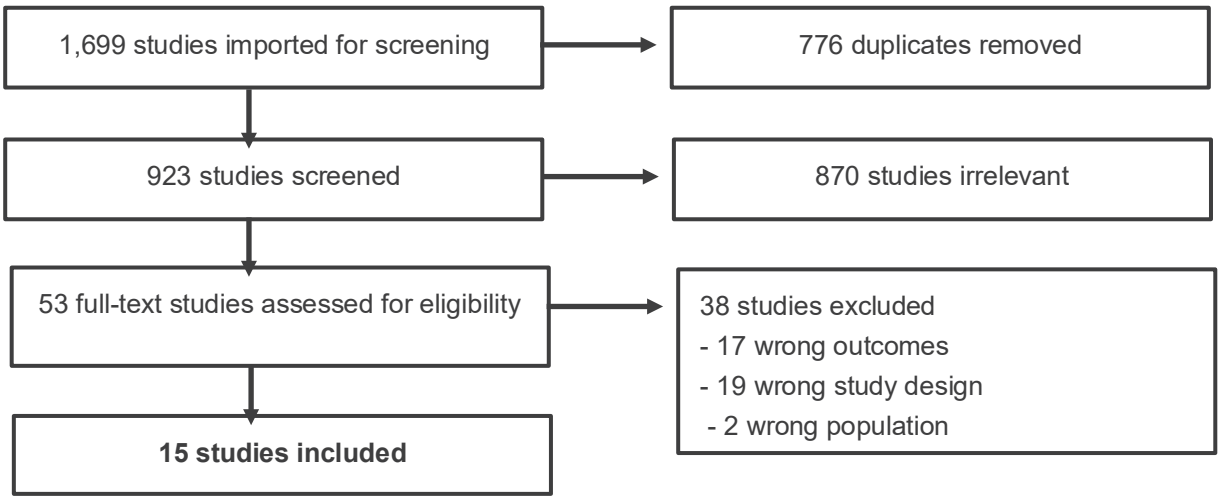

Figure 1. PRISMA flow diagram

Quality assessment

The Newcastle-Ottawa Scale (NOS) was revised and then used to assess research paper quality. Modifications included the removal of questions irrelevant to the scope of the current study, for example, *demonstration that the outcome of interest was not present at start of study* was removed as the systematic search was not limited to prospective cohort studies. Each paper was assessed using a star rating system to identify whether papers were of low, moderate or high quality, depending on selection bias, comparability bias and outcome bias. Each paper was rated out of a possible eight starts categorised as follows: 0-2 stars low quality; 3-4 stars moderate quality; and 5-8 stars high quality. All papers were evaluated by two independent reviewers (KM and AS), with discrepancies in quality ratings being resolved via discussion. Included papers ranged from moderate to high quality.

Data extraction

A single reviewer (KM) extracted the following data categories: author, year, country, sample size, gender of population (% male), sample type (e.g., recently enrolled military personnel, military personnel with BD), military unit/service branch, BD measure, and outcomes. A second reviewer (AS) checked for completeness and correctness of extracted data.

5 Results

Our search discovered 15 relevant articles which were primarily cohort studies (n = 9), with the exception of one cross-sectional study, two books, and three studies which retrospectively assessed medical records. Twelve articles included military populations from the United States and three were Swedish military personnel. Some used data from all military services and others utilised samples of personnel from the Army or Marines.

Risk factors

Summary of risk factors:

- Genetics
- IQ
- Hyperthyroidism
- Anger
- Male sex
- Personality (social maturity, mental energy, emotional stability, neuroticism)
- PTSD
- Alcohol misuse
- Deployments
- Trauma

Our search primarily discovered articles relevant to risk factors for the development of BD in military populations. Eleven articles explored risk factors including biological, cognitive, comorbid disorders, and service-related factors. Biological and cognitive factors including sex, genetic factors (Nievergelt et al., 2015; Polimanti et al., 2018; Weber et al., 2015), intelligence (Gale et al., 2013), maturity (Hayes et al., 2017), emotional stability and physical health (Zader et al., 2019) have been found to be associated with higher rates of BD. Comorbid anger (Smith et al., 2021) and PTSD (Nievergelt et al., 2015; Polimanti et al., 2018; Walker et al., 2015) were explored along with service related factors including deployment (Kessler et al., 2014).

In a prospective cohort study using a sample of over one million Swedish military personnel, Gale et al. (2013) found that risk of hospitalisation among those with BD fell as IQ increased. Men with lower IQ had increased risk of hospitalisation and men with higher intelligence had lower risk compared to men with average IQ. After excluding men with any comorbid mental health disorder (except comorbid depressive disorder) and including those with only BD or BD and one or more mood disorders, the pattern of results was similar in that men with lower intelligence had higher risk of hospitalisation compared to those with average intelligence, however unlike analyses of all men with BD, those with only BD and higher intelligence had similar or even slightly increased risk.

Thyroid disorders have been associated with mental health symptoms, most often anxiety and depression (Ittermann et al., 2015). A recent study explored the association with BD (Zader et al., 2019). In a sample of 2,480 military personnel, individuals with hyperthyroidism were 4.9 times more likely to be diagnosed with BD, with just over half being diagnosed with BD more than 90 days before their hyperthyroidism diagnosis.

Sex was also shown to be a significant factor whereby males with hyperthyroidism were more likely to have a diagnosis of BD than females with hyperthyroidism (Zader et al., 2019). The RANZCP guidelines highlight the importance of considering the biopsychosocial lifestyle model during clinical assessment for mood disorders, noting that mood disorders can be further characterised with respect to illness history and comorbidities (Malhi et al., 2021).

Personality traits have been investigated as predictors of BD (Hayes et al., 2017). In one study, traits assessed via semi-structured interviews with military psychologists included social maturity (extraversion and sense of responsibility); mental energy (tendency to take initiative, persevere and be task oriented); emotional stability (ability to control and tolerate nervousness and anxiety). Hayes et al. (2017) found increased rates of BD were associated with both low and high deviations from average social maturity. The three personality traits assessed by Hayes et al. (2017) are associated with the big five personality traits as follows: social maturity (high conscientiousness, extraversion, and agreeableness); mental energy (high conscientiousness and openness to experience); emotional stability (low neuroticism and high agreeableness). Some of the big five personality traits have been shown to be associated with resilience, physical health and suicidal ideation among current and ex-serving military personnel (Oshio et al., 2018; Stefanovics et al., 2021; Straus et al., 2019). Assessment of core personality functioning should be used to inform clinical management and those with personality dysfunction may require more intensive treatment (Malhi et al., 2021). Personality traits (particularly neuroticism) have the potential to have a bidirectional relationship with mood problems, with some evidence indicating personality can impact BD and vice versa.

Several studies detailed comorbidities with BD, including PTSD, anger, and alcohol misuse. One study found new US soldiers with either impairing or non-impairing anger attacks had increased odds of experiencing mania or hypomania compared to new soldiers who did not experience anger attacks, however, pre-enlistment anger attacks were not associated with new onset mania or hypomania (Smith et al., 2021). In a sample of US military members and veterans following mild traumatic brain injury, Walker et al. (2015) found individuals with PTSD were 11 times more likely to be diagnosed with BD. Genome-wide association studies (GWAS) have found PTSD diagnosis is associated with genetic risk for BD (Nievergelt et al., 2015), while the genetic overlap between BD and alcohol misuse is moderated by trauma exposure (Polimanti et al., 2018). The RANZCP guidelines highlight that alcohol and substance misuse are common in mood disorders which contribute to the disorder and can negatively impact treatment response, highlighting that consideration of comorbidities is important during clinical assessment. These findings also support the guidelines which describe genetic risk for BD (Malhi et al., 2021).

One US study including a sample of active-duty soldiers explored service-related factors associated with BD. Kessler et al. (2014) found that the number of deployments had a significant positive relationship with BD. Individuals with pre-enlistment BD onset were 7 times more likely to experience severe role impairment (as measured by the Sheehan Disability Scale) compared to individuals without mental health disorders, and the post-enlistment onset group were 3.8 times more likely (Kessler et al., 2014). The guidelines highlight that mood disorders among refugees and immigrants commonly cooccur due to their prior exposure to multiple traumas (Malhi et al., 2021). Given that military populations are often exposed to several traumas as part of their service, particularly during deployment, it could be theorised that PTSD is likely to co-occur with BD among this population.

Three studies explored the risk of BD diagnosis itself (Gale et al., 2012; Nock, 2016; Stein et al., 2017). Associated factors included an increased risk of death (Gale et al., 2012), suicidal ideation and attempt (Nock, 2016), and shared genetic risk for BD and suicide attempt (Stein et al., 2017). Research found that military personnel with a diagnosis of BD had up to 5.5 times higher risk of death than military personnel without the disorder (Gale et al., 2012). The guidelines suggest that suicide risk among those with BD is 30-60 times the general population (Malhi et al., 2021). Adjustment for early-life socioeconomic status, body mass index, and blood pressure had little effect on associations. The effect was somewhat attenuated after controlling for later-life socioeconomic status, IQ, and educational level, while exclusion of deaths by suicide further weakened the effect, however associations remained (Gale et al., 2012). BD has been shown to increase likelihood of experiencing suicidal ideation, as well as predict the transition from ideation to attempt (Nock, 2016). Further, studies have indicated there may be shared genetic risk between BD and suicide attempt (Stein et al., 2017).

Misdiagnosis

Literature relevant to the misdiagnosis of BD in military populations was not discovered within the search, however in consultation with an expert panel, a key theme emerged. The development of depression occurs prior to mania, often by several years, and given diagnosis of BD is grounded on the endorsement of mania, it is possible diagnosis may not occur until later in service or following transition. Further, hypomania, which is shorter in duration compared to mania, may facilitate roles within Defence and continue undetected until the development of mania and significant dysfunction. The expert panel also recognised the challenge of distinguishing adult ADHD from hypomania.

Screening tools

Our search did not reveal reliable assessment of screening tools or measures for BD in a military population, however consultation with an expert panel, including Defence Psychiatrists and clinician-researchers Professors, determined two key factors. Firstly, the veracity of reporting from individuals in the Defence force, who want to maintain their health and their career, may impact screening and diagnosis. Secondly, experts do not recommend computerised self-report screening tools due to their ability to both over and under-diagnose BD. Instead, the experts recommend frontline clinicians should be better trained in the detection and management of the disorder, noting that clinicians are best placed to use suitable prompts for the further exploration of symptoms.

Best Practice Clinical Management

The literature search returned one relevant item with description of the United States Veterans Administration and Department of Defence Clinical Practice Guidelines for PTSD, which suggest that when comorbid with PTSD, BD should be treated concurrently, however this also depends on resource availability, patient preference, and severity of symptoms (Lazar, 2014). In contrast to this, expert clinician-researchers have recommended prioritising and stabilising BD symptoms prior to the treatment of PTSD symptoms. Guidelines also recommend referral to speciality care for unstable BD (Lazar, 2014).

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