RESEARCH ARTICLE



WILEY

Anxiety, distress tolerance, and the relationship between complex posttraumatic stress disorder symptoms and alcohol use in veterans

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Funding information

Forces in Mind Trust, Grant/Award Number: FiMT17/0510S

Abstract

Objectives: Little is known about whether distress tolerance and anxiety mediate the relationship between comorbid complex posttraumatic stress disorder (CPTSD) and alcohol use among military veterans. Here, we investigated the contribution of distress tolerance and anxiety on the strength of the CPTSD and alcohol use association. We hypothesized that the impact of a two-factor model of CPTSD derived from subscale scores on the *International Trauma Questionnaire* (ITQ)—namely ITQ PTSD and ITQ Disturbances in Self Organization (DSO; e.g., issues with affective regulation/self-belief and shame)—on alcohol use severity would be mediated by anxiety but not by distress tolerance.

Methods: Participants included 403 community-dwelling United Kingdom (UK) veterans (91.64% male, $M_{\rm age}$ = 51.15 years, SD = 12.48) recruited as part of a larger, online study. **Results:** Findings indicated that the influence of CPTSD symptoms on alcohol use severity was mediated by anxiety, not by distress tolerance, with greater relative impact due to ITQ DSO status than ITQ PTSD status.

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Conclusions: We identified the mediational influence of anxiety and distress tolerance on the association between CPTSD subscales and alcohol use in UK veterans. Interventions for anxiety may be adapted for reducing problematic alcohol use and the impact of CPTSD symptoms in veterans with comorbid PTSD and alcohol use disorder.

KEYWORDS

alcohol use, anxiety, complex PTSD, disorders of self-organization, distress tolerance, veterans

1 | INTRODUCTION

Posttraumatic stress disorder (PTSD) and addictive behaviors such as alcohol use disorder (AUD) frequently co-occur in military veterans and the general population (Castillo-Carniglia et al., 2019; De Matos et al., 2018; Debell et al., 2014; McGlinchey et al., 2022; Norman et al., 2018; Smith et al., 2016). Co-occurring PTSD and AUD result in greater clinical and functional impairment than either disorder alone (Blakey et al., 2022; Simpson et al., 2020; Straus et al., 2019), and veterans with comorbid PTSD and AUD are more than three times as likely to have attempted suicide than veterans with PTSD alone (O'Laughlin et al., 2018). Veterans with PTSD-AUD are also more likely to have depression and anxiety, to be receiving mental health treatment, and to report lower cognitive-emotional functioning and diminished quality of life (O'Laughlin et al., 2018).

Several theoretical accounts have been proposed to explain comorbid PTSD and AUD, such as the disorders arising from common risk factors like adverse childhood experiences (Banducci et al., 2019), alcohol use promoting impulsivity and risk-taking which increases the risk of experiencing a traumatic event and subsequently PTSD (Chilcoat & Breslau, 1998), or the self-medication hypothesis that claims veterans use alcohol to avoid painful emotions and reminders of traumatic experiences (Black et al., 2018). Given this, it is important to develop a comprehensive understanding of the relation between PTSD and AUD to inform theoretical development and future clinical intervention. Previous studies have sought to identify which PTSD cluster is most closely associated with AUD (Palmisano et al., 2021); however, it remains unclear as to whether a specific cluster is more closely associated with AUD than others (Smith & Cotter, 2018). Recently, McGlinchey et al. (2022) conducted a symptom-level network analysis of the associations between PTSD and AUD among UK Armed Forces veterans living in Northern Ireland (NI) and determined that the PTSD symptom "reckless behavior" was most strongly associated to the alcohol use items. However, similar investigations are needed as to how the range of possible underlying cognitive-emotional mechanisms related to coping with PTSD symptoms impact on alcoHol use in veterans (Straus et al., 2019; Weiss et al., 2020).

To date, clinical research investigating PTSD in veterans has tended to adopt the definition of PTSD provided by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013). As an alternative to DSM-5, the latest revision of the *International Classification of Diseases* (ICD-11; Reed et al., 2022; World Health Organization, 2018) includes distinct, hierarchical diagnosis of complex posttraumatic stress disorder (CPTSD). According to the ICD-11, diagnosis of CPTSD requires all diagnostic requirements for PTSD to be met, with additional symptoms and impairments from a cluster of symptoms referred to as disturbances in self-organization (DSO). These DSO symptoms include severe and persistent issues with affective regulation, diminished self-belief accompanied by shame or guilt, and difficulties in sustaining relationships, which result in significant impairment in functioning. A growing literature now supports the validity of CPTSD as a distinct construct (Cloitre et al., 2020; Cyr et al., 2021; Redican et al., 2021).

The International Trauma Questionnaire (ITQ; Cloitre et al., 2018) has been shown to be a reliable and valid measure of the ICD-11 PTSD and CPTSD diagnoses across cultures (Ho et al., 2020; Karatzias et al., 2017). When assessed on data from veterans in NI, factor analytic work has demonstrated that the CPTSD symptoms cluster together across three symptom groupings (3 PTSD/3 DSO; Armour et al., 2021). Those veterans with CPTSD are also likely those who report higher rates of childhood adversity among veterans with CPTSD (Murphy et al., 2021). The ITQ is also a useful tool for tracking clinically significant treatment-related changes (Bongaerts et al., 2022; Cloitre et al., 2021) among the general population. Spikol et al. (2022) reported that veterans experiencing CPTSD were also likely to have histories of repeated/cumulative trauma and report a range of associated psychopathologies. An assessment of the relative mediational roles played by risk factors and cognitive-emotional mechanisms in the relation between ITQ-assessed CPTSD and AUD is therefore warranted (Karatzias & Cloitre, 2019).

One potential risk factor is distress tolerance (DT; Simons & Gaher, 2005) or the ability to experience yet withstand negative psychological states (Akbari et al., 2022; Vujanovic et al., 2015, 2022). Low DT has been implicated in alcohol use (Buckner et al., 2007) and post-adversity psychopathological outcomes (Robinson et al., 2021). Deficits in DT may, therefore in part account for the relationship between PTSD/CPTSD and alcohol use (Boffa et al., 2018; Brooks Holliday et al., 2016; Duranceau et al., 2014; Vujanovic et al., 2015; Zegel et al., 2019). Recently, Vujanovic et al. (2022) reported that scores on the *Distress Intolerance Index* (DII; McHugh & Otto, 2012) mediated the relationship between the severity of PTSD symptoms and substance use, but not alcohol use, in US military veterans. It remains to be seen, however, whether DT mediates the relationship between CPTSD and alcohol use among UK veterans.

Anxiety, particularly the dimensional personality trait of anxiety sensitivity (AS) or the fear of anxiety and related sensations (McNally, 2002), but also generalized anxiety disorder (GAD), have been identified as theoretically and clinically relevant factors in PTSD symptomatology (Naragon-Gainey, 2010). AS has been implicated in the development and persistence of PTSD (Zoellner et al., 2020) and AUD (Chavarria et al., 2015; Schmidt et al., 2007), and may be a contributing factor in the observed comorbidity of these disorders (Vujanovic et al., 2018). Interventions targeting AS are effective with clients with PTSD (Norr et al., 2020) which indicates a possible mediational role for PTSD and/or AUD. PTSD symptom severity is related to alcohol use via heightened AS in US veterans (Vujanovic et al., 2022), supporting a self-medicating role for increased drinking. It remains to be seen whether the broader anxiety symptom clusters captured by measures such as GAD-7 exert a similar mediational impact on alcohol use in veterans with CPTSD to that which has been shown by AS.

The present study therefore sought to investigate, for the first time, whether DT and anxiety mediated the relationship between CPTSD and alcohol use among UK Armed Forces veterans. We hypothesized that the impact of a two-factor model of CPTSD derived from subscale scores on the ITQ—namely ITQ PTSD and ITQ DSO - on alcohol use severity would be mediated by anxiety but not by DT.

2 | MATERIALS AND METHODS

2.1 | Participants and procedure

Armed Forces veterans living in the UK were recruited as part of a larger study (Dighton et al., 2023). Veterans who provided a valid service number and had emigrated since leaving the Armed Forces were also included (2.09% of the sample). The final sample comprised 403 veterans who completed at least one question on each of the measures. Veterans were predominantly male (91.64%) with a mean age of 51.15 years (SD = 12.48). Further details of the sample are available in Supplementary Materials.

The study protocol was reviewed and received ethical approval by - Wales NHS Research Ethics Committee 6 (REC reference 19/WA/0134) and was conducted in accordance with STROBE guidelines (Vandenbroucke, 2007). All procedures comply with the ethical standards of the relevant national and institutional committees on human

experimentation and with the Helsinki Declaration of 1975/2008. Participants were reimbursed with a £10 shopping voucher on completion of the study.

2.2 | Measures

The International Trauma Questionnaire (ITQ; Cloitre et al., 2018) is an 18-item measure for the diagnosis of PTSD and complex PTSD (CPTSD) based on ICD-11. The ITQ is comprised of four sections, with the first two sections determining probable PTSD, and the second two sections identifying CPTSD. In the first section, questions relate to three PTSD symptom clusters: re-experiencing in the here and now, avoidance, and sense of current threat. The second section asks whether the above problem has affected any of three life domains and relates to functional impairment from PTSD. The third section questions relate to symptoms from three DSO clusters: affective dysregulation, negative self-concept, and disturbances in relationships. The final section asks how the emotions identified in the third section may have affected three domains of life relate to functional impairment from CPTSD. Respondents use a 5-point scale to indicate their responses, from 0 ("Not at all") to 4 ("Extremely"). For a diagnosis of PTSD, respondents must score greater than, or equal to 2 for each PTSD symptom cluster, and above this threshold on the PTSD functional impairment section. In addition, for a diagnosis of CPTSD, respondents must score greater than, or equal to 2 for each DSO symptom cluster, and above this threshold on the DSO functional impairment section. Respondents can receive either a potential diagnosis of PTSD or CPTSD, not both. In the current study, the ITQ PTSD and ITQ DSO scores both demonstrated excellent internal consistency (PTSD: Cronbach's α = .93, 95% confidence interval [CI] [0.92–0.94]; DSO: α = .95, 95% CI [0.94–0.95]).

The Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001) is a 10-item screening tool to measure harmful alcohol consumption within the past year. Items were scored from 0 to 4 as measures of the frequency and quantity of alcohol consumed. Higher scores reflect more problematic alcohol consumption. In the present study, the Cronbach's α was .88, 95% CI (0.85–0.89).

The Generalized Anxiety Disorder Assessment (GAD-7; Spitzer et al., 2006) is a 7-item measure for generalized anxiety disorder. Items are scored using a 4-point scale ranging from 0 ("not at all") to 3 ("nearly every day") assessing frequency of symptoms in the past 2 weeks. In the current study, the internal consistency of the GAD-7 total score was excellent (Cronbach's $\alpha = .94, 95\%$ CI [0.92–0.95]).

The Distress Tolerance Scale (DTS; Simons & Gaher, 2005) is a 15-item self-report measure of an individual's ability to tolerate psychological distress. Respondents use a 5-point scale ranging from 1 ("Strongly agree") to 5 ("Strongly disagree"). In addition to a total score, the DTS also yields four subscale scores: tolerance, appraisal, absorption of attention, and efforts to regulate distress. The internal consistency of the DTS total score in the present study was excellent (Cronbach's α = .94, 95% CI [0.94–0.95]), while the internal consistency for the subscales was good (Tolerance α = .80 [0.76–0.84], Appraisal α = .87 [0.86–0.90], Absorption α = .85 [0.81–0.87], and Regulation α = .80 [0.76–0.84]).

2.3 Data analytic plan

All analyses were conducted using *R* version 4.1.2 (R Core Team, 2021). Missing data were examined using Little's (1988) Missing Completely At Random (MCAR) test, to determine whether data are not missing completely at random. Descriptive statistics and zero-order correlations were calculated for all measures based on the total scores.

The indirect associations (*ab* pathways) of ITQ PTSD score and ITQ DSO score (X's) on AUDIT total score (Y) via GAD-7 and DTS (M's) were estimated using bootstrapping procedures implemented in the *psych* package in *R* (Revelle, 2021). The model also yields estimates for the associations between X and M (*a* paths), the associations

between M and Y, controlling for X (the *b* pathways), as well as the direct associations of X on Y (the *c* paths) and the total associations between X's and Y (the *c*' pathways—which are the sum of the direct [*c*] and indirect [*ab*] effects). With two predictor variables (X's) and two mediation variables (M's) we can also directly compare the magnitude of *ab* estimates to determine whether any of the indirect effects differ in magnitude or direction. The 95% confidence intervals around the indirect associations and their comparisons were generated using bias-corrected bootstrap procedures with the recommended 5000 resamples (Hayes, 2012). For the indirect effects and their respective comparisons, effects for which the 95% Cls do not include zero are considered statistically significant (Preacher & Hayes, 2004).

3 | RESULTS

3.1 Descriptive analyses and correlations

Missing data at the item level ranged from 0% to 0.74% and Little's MCAR test did not indicate that data were missing non-randomly, χ^2 = 552.14 (588), p = .853. As such, missing data were handled with listwise deletion which is deemed to be an acceptable and unbiased method for dealing with missing data under such circumstances (Cheema, 2014; McKnight et al., 2007). Of the n = 403, 20 participants had missing data in one or more measures and were therefore excluded from all analyses. The final analyzed sample therefore included 383 veterans. Descriptive statistics and zero-order correlations are shown in Table 1 and the proportion of participants in each diagnostic category are shown in Table 2. See Supplementary Materials for descriptive statistics for the DTS subscales.

The correlations between all total score measures were statistically significant, even after adjusting for multiple comparisons (using the false discovery rate correction; Benjamini & Hochberg, 1995). The ITQ PTSD, ITQ DSO,

 TABLE 1
 Descriptive statistics and zero-order correlations for all total score measures.

	ITQ PTSD	ITQ DSO	GAD-7	DTS	AUDIT
ITQ PTSD					
ITQ DSO	.75****				
GAD-7	.71****	.78****			
DTS	61****	65***	66****		
AUDIT	.24***	.21****	.27****	18***	
Mean	6.76	7.9	5.45	3.3	9.42
SD	6.17	6.76	5.58	0.99	7.44
95% CI	[6.15-7.36]	[7.2-8.62]	[4.93-6.03]	[3.2-3.4]	[8.66-10.18]
Range	0-24	0-24	0-21	1-5	0-32
Skewness	0.76	0.57	1	-0.14	0.85
Kurtosis	2.59	2.14	3.13	2.17	3.11

Note: The 95% confidence intervals were calculated using the bias-corrected and accelerated bootstrap procedure. ****p < 0.0001, ***p < 0.001, **p <

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test total score; DTS, Distress Tolerance Scale total score; GAD-7, Generalized Anxiety Disorder scale total score; ITQ PTSD, International Trauma Questionnaire PTSD total score; ITQ DSO, International Trauma Questionnaire Disturbances in Self-Organization total score.

TABLE 2 Percentage, number of participants (n) in each category, and scoring range for the ITQ, AUDIT, and GAD-7.

	Category	Percentage	n	Range
ΙΤΟ	"Likely PTSD"	4.18	16	ITQ PTSD: 9-22 ITQ DSO: 5-17
	"Likely CPTSD"	17.23	66	ITQ PTSD: 9-24 ITQ DSO: 9-24
AUDIT	"Non-drinkers"	10.44	40	0-0
	"Lower risk"	34.73	133	1-7
	"Increasing risk"	35.51	136	8-15
	"Higher risk"	7.05	27	16-19
	"Possible alcohol dependence"	12.27	47	20-32
GAD-7	"No anxiety"	51.44	197	0-4
	"Mild anxiety"	26.63	102	5-9
	"Moderate anxiety"	11.75	45	10-14
	"Severe anxiety"	10.18	39	15-21

Note: See Supporting Information Materials for descriptive statistics for the DTS subscales.

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test total score; CPTSD, complex posttraumatic stress disorder; DTS, Distress Tolerance Scale total score; GAD-7, Generalized Anxiety Disorder scale total score; ITQ, International Trauma Questionnaire; PTSD, posttraumatic stress disorder.

GAD-7, and AUDIT total scores were all strongly positively correlated with each other, with weaker correlations with the AUDIT for all measures (Table 2). Conversely, the DTS was negatively correlated with the ITQ PTSD, ITQ DSO, GAD-7, and AUDIT total scores; this is likely a result of the DTS indexing the magnitude of distress tolerance, rather than distress *intolerance* per se.

3.2 | Mediation analysis

A graphical summary of the mediation analysis is presented in Figure 1. With direct effects (c'-traditional regression analyses), only the GAD-7 total score was a statistically significant predictor of AUDIT (B = .305, t(378) = 2.65, p = .008). While ITQ PTSD total score (B = .135, t(378) = 1.42, p = .158), ITQ DSO total score (B = -.044, t(378) = 0.45, p = .654) and DTS total score (B = .089, t(378) = 0.170, p = .865) were not statistically significant predictors of the AUDIT scores. For the total effects (c) ITQ PTSD score was a statistically significant predictor of AUDIT scores (B = .211, t(380) = 2.34, p = .02), while ITQ DSO scores were not significantly associated with AUDIT total scores (B = .092 t(380) = 1.12, p = .262). In terms of the "a" pathways (the effect of the independent variables on the mediating variables) both ITQ PTSD and ITQ DSO scores were statistically significant predictors of the GAD-7 (ITQ PTSD on GAD-7: B = .263, t(380) = 6.35, p < .001; ITQ DSO on GAD-7: B = .466, t(380) = 12.35, p < .001) and the DTS (ITQ PTSD on DTS: B = -.045, t(380) = 4.895, p < .001; ITQ DSO on DTS: B = -.065, t(380) = 7.875, p < .001). For the "b" pathways (the effect of the mediating variables on the dependent variable, controlling for the independent variables), GAD-7 was a statistically significant predictor of the AUDIT total score (GAD-7 on AUDIT: B = .305, t(378) = 2.651, p = .008), while DTS was not (DTS on AUDIT: B = .089, t(378) = 0.170, p = .865).

Crucially, both ITQ PTSD (B = .082, 95% CI [0.012–0.168]) and ITQ DSO scores (B = .144, 95% CI [0.026–0.267]) exhibited indirect effects on AUDIT total score via GAD-7 ("ab" pathways). By contrast, neither

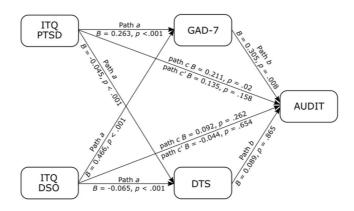


FIGURE 1 Graphical summary of the mediation analysis. AUDIT, Alcohol Use Disorders Identification Test total score; DTS: Distress Tolerance Scale total score; GAD-7, Generalized Anxiety Disorder scale total score; ITQ DSO, International Trauma Questionnaire Disturbances in Self-Organization total score; ITQ PTSD, International Trauma Questionnaire PTSD total score.

of the indirect effects on AUDIT total score via DTS can be considered statistically significant (PTSD: B = -.004, 95% CI [-0.052 to 0.041]; ITQ DSO: B = -.005, 95% CI [-0.071 to 0.061]). Finally, comparison of the magnitude of the association between ITQ PTSD and ITQ DSO scores, respectively, and AUDIT via GAD-7 indicates that the indirect effect is larger for the latter than for the former (mean difference = 0.061, 95% CI [0.005-0.140]). None of the other comparisons of the indirect effects were statistically significant (Supporting Information Materials). The full model, which accounted for 8% of the variance in AUDIT total scores, was statistically significant (F(4.378) = 7.923, p < .001, $R^2 = .08$).

As shown in Supporting Information (Tables S5 and S6), further sub-group analyses were conducted with low (< 8) and high-scoring groups (> 8) for the GAD-7, respectively. The sensitivity analyses revealed an effect for low anxiety but not high anxiety scores, thus confirming that our findings were modulated by anxiety symptoms.

4 | DISCUSSION

The present study sought to extend existing findings on the association between DT, anxiety, CPTSD subscales (PTSD & DSO), and AUD among UK Armed Forces veterans. Our main hypothesis was supported; that is, we identified that the relative impact of ITQ-assessed PTSD and DSO symptom clusters on alcohol use severity was mediated by anxiety but not by DT. This extends previous findings from US veterans (Vujanovic et al., 2022) on the mediational influence of the CPTSD and alcohol use relationship to alternative measures of both anxiety and DT. Moreover, this central finding encapsulates, for the first time, a broad range of ITQ PTSD symptomatology based on ICD-11 criteria and revealed that ITQ DSO status exerted a greater impact than ITQ PTSD status on alcohol use via anxiety. Taken together, these findings have implications for the clinical assessment and treatment of CPTSD and AUD in veterans and supports a burgeoning research literature on the mediational variables affecting these disorders in vulnerable groups (Armour et al., 2021; Frost et al., 2022; Karatzias et al., 2021).

We found that anxiety had a greater impact of the relationship between the two subscales of CPTSD compared to the impact of DT. Differences in magnitude exerted by CPTSD that were identified here may stem from the broader, adverse effects of the PTSD diagnosis on self-organization and/or the long-term impacts of coping with traumatic experience. Indeed, the three CPTSD symptom clusters may uniquely contribute to impaired and/or elevated anxiety levels related to prior military traumatic experience and subsequent drinking. This is consistent with research from treatment seeking veterans with CPTSD who reported a greater mental health burden, including

elevated anxiety, and impaired general functioning (Murphy et al., 2021) likely to prompt increased alcohol use (Leightley et al., 2022). Further research is needed to disentangle the relative contribution of CPTSD to anxiety and alcohol use among veterans.

It would be useful for future work to evaluate the potential mediational role of other variables in alcohol use severity among veterans and the time course of change following clinical treatment (Feingold & Zerach, 2021). Recently, Carvalho et al. (2022) tested a novel model of combat-related PTSD and found a key role for uncompassionate self-responding and experiential avoidance in mediating PTSD symptomatology. Experiential avoidance is involved when reminders of traumatic experiences prompt elevated anxiety and lead to increased drinking as a means of escaping or avoiding the unpleasant emotional consequences (Chawla & Ostafin, 2007). Specifically, it was noted that experiential avoidance and uncompassionate self-responding both mediated effects of noncombat threat-related memories and depersonalization/derealization processes on PTSD, with experiential avoidance alone mediating the impact of combat-related exposure distress. The generalizability of such findings to the DSO symptom clusters, which are known to have stable psychometric properties and accurately identify individuals meeting the diagnostic criteria for CPTSD (Shevlin et al., 2018), would be salutary in better understanding their role with diverse trauma samples and with alternative measures of common emotion regulation processes such as experiential avoidance.

Our correlational analyses found that ITQ PTSD and ITQ DSO scores predicted anxiety and DT. To our knowledge, these are the first such findings obtained with the DTS and complement previous findings obtained with the DII. For instance, Vujanovic et al. (2022) found that scores on the DII mediated the relationship between the severity of PTSD symptoms and substance use, but not alcohol use, in US military veterans. By contrast, we found that not only was PTSD/CPTSD status associated with DT but that scores on the DTS mediated the impact of both PTSD and CPTSD on alcohol use. Substance use was not assessed here but our findings add weight to the argument that diminished DT is implicated in alcohol use (Buckner et al., 2007) and impacts on the relationship between PTSD and severity of alcohol use (Brooks Holliday et al., 2016; Duranceau et al., 2014). Given that we have confirmed a key role for DT in mediating the impact of PTSD symptoms on alcohol use, further work should seek to determine its potential as a target for the treatment (Boffa et al., 2018; Vujanovic et al., 2015).

There are potential limitations that warrant further research. First, although Vujanovic et al. (2022)—the study on which the present approach was based—also employed a cross-sectional design, it is often argued that these designs are ill-suited to mediation analyses and prevent causal inferences from being made (O'Laughlin et al., 2018). While it is beyond the remit of the present study to comment on this debate, it would be helpful for future to employ longitudinal or prospective designs to identify potential bidirectional effects. Second, as we employed different measures of DT, anxiety, and PTSD/CPTSD to those seen in the extant literature, further studies are needed to determine robustness. Also, the potential treatment-seeking basis of our community-dwelling sample should be fully considered given that veterans have higher healthcare costs than matched non-veterans (Harris et al., 2021) and report higher rates of PTSD and CPTSD (Dighton et al., 2023; Murphy et al., 2021).

5 | CONCLUSION

In conclusion, we investigated the mediational influence of anxiety and DT on the relationship between CPTSD subscales and alcohol use in UK veterans. Implications of the findings include the potential usefulness of interventions established for anxiety being adapted for reducing problematic alcohol use and the incorporation of clinical outcome targets involving reduced anxiety as alternative assessments for the efficacy of intervention in veterans with comorbid PTSD-AUD.

ACKNOWLEDGMENTS

We thank the UK Armed Forces charities and veterans' networks for their keen support of this research. This work was supported by a grant from Forces in Mind Trust (FiMT17/0510S).

The authors declare no conflict to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study protocol was reviewed by NHS Wales REC 6 and was conducted in accordance with STROBE guidelines.

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PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1002/jclp.23604.

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How to cite this article: Whiteford, S., Quigley, M., Dighton, G., Wood, K., Kitchiner, N., Armour, C., & Dymond, S. (2023). Anxiety, distress tolerance, and the relationship between complex posttraumatic stress disorder symptoms and alcohol use in veterans. *Journal of Clinical Psychology*, 1–12.

https://doi.org/10.1002/jclp.23604