

## Short Report

# Subthreshold post-traumatic stress disorder as a risk factor for post-traumatic stress disorder: results from a sample of USA veterans

Robert H. Pietrzak, Frances G. Javier, John H. Krystal and Steven M. Southwick

Subthreshold post-traumatic stress disorder (PTSD) is more prevalent than PTSD, yet its role as a potential risk factor for PTSD is unknown. To address this gap, we analysed data from a 7-year, prospective national cohort of USA veterans. Of veterans with subthreshold PTSD at wave 1, 34.3% developed PTSD compared with 7.6% of trauma-exposed veterans without subthreshold PTSD (relative risk ratio 6.4). Among veterans with subthreshold PTSD, specific PTSD symptoms, greater age, cognitive difficulties, lower dispositional optimism and new-onset traumas predicted incident PTSD. Results suggest that preventive

interventions targeting subthreshold PTSD and associated factors may help mitigate risk for PTSD in USA veterans.

**Keywords**

Epidemiology; post-traumatic stress disorder; military psychiatry; nosology; trauma.

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Subthreshold post-traumatic stress disorder (PTSD), which is not a recognised diagnostic entity, is highly prevalent in trauma-exposed civilian and military populations worldwide, often two to three times more prevalent than PTSD. For example, a nationally representative study of USA veterans found that 22.1% met criteria for subthreshold PTSD in their lifetimes and 13.5% in the past month, which was substantially higher than the 8% and 4.5% prevalence of lifetime and past-month PTSD, respectively.<sup>1</sup> In addition to being prevalent, subthreshold PTSD is associated with compromised mental and physical health, as well as functional impairment.<sup>2</sup> A recent meta-analysis found that, relative to trauma-exposed individuals without PTSD symptoms, those with subthreshold PTSD had elevated rates of psychiatric comorbidities, such as depressive symptoms, suicidality and substance abuse; reduced social and occupational functioning; and greater utilisation of healthcare services.<sup>3</sup> Subthreshold PTSD is also linked to higher rates of suicidal ideation above and beyond the effect of major depressive disorder.<sup>4</sup>

Despite the robust association of subthreshold PTSD with psychiatric comorbidities, suicidality and functional impairment, it has generally been ignored both in clinical settings and in the context of compensation.<sup>5</sup> To date, it remains unknown whether subthreshold PTSD may represent a risk factor for the development of PTSD in representative samples, and which factors may predict the conversion from subthreshold PTSD to PTSD. Given the chronicity, impairment and high cost associated with treating PTSD, examining whether subthreshold PTSD is a potential risk factor for PTSD could help inform prognostic models of PTSD and population-based prevention efforts to mitigate risk of developing this disorder.

**Method****Sample**

Data were analysed from the National Health and Resilience in Veterans Study (NHRVS), a 7-year, nationally representative, prospective cohort study of 3157 USA veterans. The sample was obtained from KnowledgePanel, a survey research panel representing approximately 98% of USA households that is maintained by GfK Custom Research (now Ipsos). A baseline (i.e. wave 1) survey was conducted in 2011 and follow-up surveys were conducted in

2013, 2015 and 2018. A total of 2305 (73%) veterans completed at least one follow-up assessment (mean number of follow-up assessments 2.2, s.d. 0.8, range 1–3 assessments). The Trauma History Screen<sup>6</sup> and PTSD Checklist–Specific Stressor Version (PCL-S)<sup>7</sup> were administered to assess trauma history and PTSD symptoms (see Table 1). Several sociodemographic, military, health and psychosocial variables associated with PTSD<sup>8,9</sup> were assessed as potential determinants of PTSD in veterans with subthreshold PTSD at wave 1, over the 7-year study period (Table 1). Wave 1 and follow-up PCL-S data were available for a total of 2155 veterans. Post-stratification weights were applied in inferential analyses, to permit generalisability of results to the USA veteran population.

**Ethics statement**

The NHRVS was approved by the Human Subjects Subcommittee of the VA Connecticut Healthcare System (protocol number RP0002). All participants provided informed consent.

**Assessments**

The DSM-IV version of the PCL-S was used to assess PTSD symptoms related to veterans' 'worst' traumatic event as assessed by the Trauma History Screen at wave 1. The most prevalent worst traumatic events among veterans with subthreshold PTSD were life-threatening illness or injury (23.5%), sudden death of a close family member or friend (21.8%) and military-related trauma (8.8%). PTSD symptom endorsement was operationalized as reporting being bothered 'moderately', 'quite a bit' or 'extremely', by the symptom. Subthreshold PTSD was classified as meeting symptom criteria for cluster B (re-experiencing) plus cluster C (avoidance) or D (hyperarousal), or those who met criteria for cluster B plus at least one cluster C and one cluster D symptom.<sup>1,3</sup> In waves 2–4, the DSM-5 version of the PCL (PCL-5)<sup>10</sup> was used to assess PTSD symptoms related to veterans' worst traumatic event endorsed at baseline. Incident PTSD was defined as meeting DSM-5 criteria A (stressor), B (intrusion symptoms), C (avoidance), D (negative mood and cognitions), E (hyperarousal), F (duration; additional question added to the PCL-5: 'How long did these reactions last?', with criterion F met if symptoms lasted >1 month) and G (clinically significant distress/functional impairment; additional question added to the PCL-5: 'Did these reactions cause you distress or result in a failure to fulfill obligations at

**Table 1** Demographic, trauma and clinical characteristics by post-traumatic stress disorder (PTSD) status over the 7-year follow-up period

	No PTSD during follow-up, <i>n</i> = 1941 (89.1%)	PTSD during follow-up, <i>n</i> = 214 (10.9%)	Test of difference	<i>P</i> -value
Wave 1 PTSD status, <sup>a</sup> <i>n</i> , weighted %			236.01	<0.001
Trauma-exposed control	1844 (92.4%)	139 (7.6%)		
Subthreshold PTSD	74 (65.7%)	38 (34.3%)		
Full PTSD	23 (45.7%)	37 (54.3%)		
Age, weighted mean (s.d.)	62.1 (14.0)	53.4 (14.8)	8.53	<0.001
Male gender, <i>n</i> (weighted %)	1769 (91.8%)	178 (86.5%)	6.60	0.010
White race/ethnicity, <i>n</i> (weighted %)	1666 (79.3%)	158 (64.5%)	24.20	<0.001
Married/partnered, <i>n</i> (weighted %)	1547 (75.1%)	163 (72.9%)	0.49	0.48
College graduate or higher education, <i>n</i> (weighted %)	897 (32.6%)	63 (22.8%)	8.58	0.003
Household income ≥US\$60 000/year, <i>n</i> (weighted %)	1062 (47.1%)	106 (46.9%)	0.23	0.63
Combat veteran, <i>n</i> (weighted %)	654 (31.2%)	91 (45.3%)	11.80	0.001
Number of lifetime traumas at wave 1, weighted mean (s.d.)	3.0 (2.5)	5.4 (3.7)	12.59	<0.001
Traumas since wave 1, weighted mean (s.d.)	1.9 (1.2)	4.2 (2.6)	22.22	<0.001
Lifetime major depressive disorder at wave 1, <i>n</i> (weighted %)	228 (11.3%)	97 (48.4%)	203.34	<0.001
Lifetime PTSD at wave 1, <i>n</i> (weighted %)	71 (3.4%)	56 (30.8%)	238.82	<0.001
Lifetime alcohol or drug use disorder at wave 1, <i>n</i> (weighted %)	356 (18.8%)	80 (38.8%)	45.67	<0.001
Loneliness at wave 1, weighted mean (s.d.)	4.3 (1.7)	6.0 (2.2)	13.99	<0.001
Cognitive functioning at wave 1, weighted mean (s.d.)	92.2 (11.0)	72.6 (25.9)	20.13	<0.001
Number of medical conditions at wave 1, weighted mean (s.d.)	2.5 (1.9)	3.2 (2.4)	4.90	<0.001
Dispositional optimism at wave 1, weighted mean (s.d.)	4.9 (1.4)	4.0 (1.8)	8.02	<0.001
Purpose in life at wave 1, weighted mean (s.d.)	21.7 (4.1)	18.2 (6.0)	11.05	<0.001
Perceived social support at wave 1, weighted mean (s.d.)	19.8 (4.8)	16.3 (5.5)	10.02	<0.001

The Trauma History Screen was used to assess exposures to 13 potentially traumatic life event types, with the option to additionally endorse an 'other' event.<sup>6</sup> An adapted lifetime version of the PTSD Checklist-Specific Stressor Version was used to assess lifetime PTSD (criteria A-F).<sup>7</sup> Adapted modules from the Mini Neuropsychiatric Interview were used to assess lifetime major depressive, alcohol and drug use disorders.<sup>11</sup> The Three-Item Loneliness Scale was used to assess loneliness; scores on each item range from 1 (hardly ever) to 3 (often), and are summed to yield a total score ranging from 3–9, with higher scores reflecting greater loneliness.<sup>12</sup> The Medical Outcomes Study Cognitive Functioning Scale-Revised was used to assess cognitive functioning; scores range from 0 to 100, with lower scores indicating worse cognitive functioning.<sup>13</sup> A Medical Conditions Checklist derived from the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV<sup>14</sup> was used to assess the presence/absence of 20 healthcare professional-diagnosed medical conditions (e.g. diabetes, heart disease, migraine); a higher number of conditions indicates greater medical burden. The following item from the Life Orientation Test-Revised was used to assess dispositional optimism ('In uncertain times, I usually expect the best'); scores range from 1 (strongly disagree) to 7 (strongly agree).<sup>15</sup> The Purpose in Life Test-Short Form was used to assess purpose in life; scores range from 4 to 28, with higher scores indicating greater purpose in life.<sup>16</sup> An abbreviated five-item version of the Medical Outcome Study Social Support Scale was used to assess perceived social support; scores range from 5 to 25, with higher scores indicating greater perceived social support.<sup>17</sup>

a. Row percentages are shown for wave 1 PTSD status; percentages for all other variables are column percentages.

home, work, or school? Endorsement of 'moderately', 'quite a bit' or 'extremely' was indicative of meeting criterion G).

## Data analysis

Chi-squared analyses and independent samples *t*-tests were conducted to compare demographic, trauma and clinical characteristics of veterans with and without PTSD over the 7-year follow-up period. Multivariable binary logistic regression analyses were then conducted in veterans with subthreshold PTSD at wave 1, to evaluate specific PTSD symptoms associated with incident PTSD (backward Wald estimation method); and sociodemographic, military, health and psychosocial determinants of incident PTSD (see Table 1 for variables included in this analysis). Relative importance analyses,<sup>18</sup> which partition explained variance among independent variables while accounting for intercorrelations among them, were then conducted to determine the relative variance in incident PTSD that was explained by significant predictors in these analyses.

## Results

Table 1 shows demographic, trauma and clinical characteristics of the sample by PTSD status over the 7-year follow-up period. In the full sample, a total of 214 veterans (weighted 10.9%) screened positive for full PTSD at one or more follow-up assessments over the 7-year follow-up period. As shown in Table 1, of the veterans with subthreshold PTSD at wave 1 (*n* = 112, 5.3% of the wave 1 cohort), 34.3% developed PTSD at one or more assessments, relative to 7.6% of trauma-exposed veterans without subthreshold PTSD (*n* = 1983, 90.6% of the wave 1 cohort, relative risk ratio 6.4, 95% CI 4.1–9.9, *P* < 0.001); of veterans with full PTSD at wave 1 (*n* = 60,

4.1% of the wave 1 cohort), 54.3% screened positive for full PTSD at one or more follow-up assessments.

In analyses excluding veterans with lifetime PTSD (*n* = 127, 6.4% of the wave 1 cohort), veterans with subthreshold PTSD at wave 1 had comparably elevated risk of incident PTSD over the follow-up period (34.1% *v.* 6.3%; relative risk ratio 7.6, 95% CI 4.7–12.3); and in an analysis adjusted for wave 1 PTSD, major depressive disorder and alcohol and drug use disorder, wave 1 subthreshold PTSD was associated with a five-fold greater likelihood of developing PTSD over the follow-up period (relative risk ratio 5.0, 95% CI 3.1–8.1).

Among veterans with subthreshold PTSD at wave 1, positive endorsement of three PTSD symptoms emerged as independent predictors of incident PTSD: psychogenic amnesia (i.e. 'trouble remembering important parts of trauma'; relative risk ratio 5.44, 95% CI 1.43–20.67), hypervigilance (i.e. 'being super alert or watchful or on guard'; relative risk ratio 3.98, 95% CI 1.52–10.40) and trauma-related nightmares (i.e. 'repeated, disturbing dreams of trauma'; relative risk ratio 2.98, 95% CI 1.07–8.26). The total model *R*<sup>2</sup> was 0.31; hypervigilance (41.8% relative variance explained) explained most of the variance in incident PTSD, and psychogenic amnesia (32.2% relative variance explained) and trauma-related nightmares (26% relative variance explained) explained the remainder of the variance in this outcome.

Among veterans with subthreshold PTSD at wave 1, greater age (relative risk ratio 1.05, 95% CI 1.01–1.10), number of traumas since wave 1 (relative risk ratio 1.22, 95% CI 1.11–2.11) and cognitive difficulties (relative risk ratio 1.03, 95% CI 1.01–1.06) at wave 1 were independently associated with increased risk for developing PTSD, whereas greater dispositional optimism at wave 1 was associated with reduced risk of developing PTSD (relative risk ratio 0.61, 95% CI 0.43–0.88). The total model *R*<sup>2</sup> was 0.37; greater number of traumas since wave 1 (65.5% relative variance explained) explained

the majority of variance in incident PTSD, whereas cognitive difficulties (18% relative variance explained), dispositional optimism (12.2% relative variance explained) and age (4.3% relative variance explained) explained the remainder of the variance in this outcome.


## Discussion

Using data from a nationally representative sample of USA veterans, results of this study provide evidence for the potential prognostic utility of subthreshold PTSD, and identify targets for population-based preventive interventions for PTSD in this population. Results revealed that subthreshold PTSD, which was more prevalent than full PTSD at baseline (5.3% *v.* 4.1%), was associated with a more than six-fold greater likelihood of developing PTSD over a 7-year follow-up period. Further, among veterans with subthreshold PTSD, hypervigilance, psychogenic amnesia and trauma-related nightmares were associated with significantly increased risk for the development of full PTSD. This finding suggests that greater sensitisation to trauma and possibly the emergence/exacerbation of PTSD symptoms in late life<sup>19</sup> may, in part, drive the development of PTSD in veterans with subthreshold PTSD. It further underscores the importance of assessing individual PTSD symptoms across symptom clusters in predicting risk for this disorder in this population.

Among veterans with subthreshold PTSD at wave 1, greater age, cognitive difficulties and lower dispositional optimism at wave 1, and increased trauma burden over the follow-up period, were associated with increased risk of developing PTSD. Increased trauma burden over the follow-up period explained nearly two-thirds of the variance in incident PTSD, which suggests that subthreshold PTSD may sensitise veterans to the deleterious effects of new-onset traumatic life events, which in turn increases risk of developing full PTSD; alternatively, new-onset traumas may give rise to PTSD in relation to a new traumatic event. Collectively, these results suggest that efforts to assess, monitor and treat negative psychological effects of trauma, mitigate cognitive difficulties and promote dispositional optimism<sup>20–22</sup> may help mitigate risk of developing PTSD in veterans with subthreshold PTSD.

Limitations of this study include the assessment of measures via a web-based platform that relied on self-report data; and its focus on a demographically homogeneous sample of USA veterans. Further research, using clinician-administered diagnostic interviews in more diverse samples, is needed to evaluate the generalisability of the results reported herein.

Notwithstanding these limitations, results of this study suggest that subthreshold PTSD may represent a risk factor for PTSD, as it was associated with a more than six-fold greater likelihood of developing PTSD. They further underscore the importance of pursuing replication of these results in other samples, using clinical interviews and DSM-5- and ICD-11-based definitions of subthreshold PTSD; raising awareness of subthreshold PTSD and related syndromes, such as adjustment disorder, as potential risk factors for PTSD; and evaluating the efficacy of targeted preventive interventions to help reduce risk for the more chronic, difficult-to-treat and costly manifestation of full PTSD in veterans and other trauma-affected populations.

**Robert H. Pietrzak** , PhD, MPH, US Department of Veterans Affairs National Center for Posttraumatic Stress Disorder, VA Connecticut Healthcare System, Connecticut, USA; and Department of Psychiatry, Yale School of Medicine, Connecticut, USA; **Frances G. Javier**, MD, US Department of Veterans Affairs National Center for Posttraumatic Stress Disorder, VA Connecticut Healthcare System, Connecticut, USA; and Department of Psychiatry, Yale School of Medicine, Connecticut, USA; **John H. Krystal**, MD, US Department of Veterans Affairs National Center for Posttraumatic Stress Disorder, VA Connecticut Healthcare System, Connecticut, USA; and Department of Psychiatry, Yale School of Medicine, Connecticut, USA; **Steven M. Southwick**, MD, US Department of

Veterans Affairs National Center for Posttraumatic Stress Disorder, VA Connecticut Healthcare System, Connecticut, USA; and Department of Psychiatry, Yale School of Medicine, Connecticut, USA

**Correspondence:** Robert H. Pietrzak. Email: robert.pietrzak@yale.edu

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## Data availability

The data that support the findings of this study are available upon reasonable request from the corresponding author, R.H.P. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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## Author contributions

R.H.P., J.H.K. and S.M.S. designed the National Health and Resilience in Veterans Study and acquired funding. R.H.P. conducted the data analyses. R.H.P., F.J.G. and S.M.S. conceptualised the study and drafted the initial version of the manuscript. All authors interpreted the results, provided critical revisions of the manuscript and approved the final version.

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## Declaration of interest

None.

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## psychiatry in literature

### Epidemics: A Journal of the Plague Year, London, 1665 – by Daniel Defoe

Greg Wilkinson 

Defoe relates that at the beginning of December 1664, two men, said to be French, died of plague at the upper end of Drury Lane. While ‘knavery and collusion’ underestimated mortality, panic set in from mid-1665:

[T]he richer sort of people, especially the nobility and gentry from the west part of the city, thronged out of town with their families and servants [...] nothing was to be seen but waggons and carts, with goods, women, servants, children, &c.; coaches [...] all hurrying away [...].

[T]here was no getting at the Lord Mayor’s door [...] there were such pressing and crowding there to get passes and certificates of health for such as travelled abroad, for without these there was no being admitted to pass through the towns upon the road, or to lodge in any inn [...].

All the plays and interludes [...] were forbid to act; the gaming-tables, public dancing-rooms, and music-houses, which multiplied and began to debauch the manners of the people, were shut up and suppressed; and the jack-puddings, merry-andrews, puppet-shows, rope-dancers, and such-like doings, which had bewitched the poor common people, shut up their shops, finding indeed no trade; for the minds of the people were agitated with other things, and a kind of sadness and horror at these things sat upon the countenances even of the common people. Death was before their eyes, and everybody began to think of their graves, not of mirth and diversions.

[I]t was seldom that the weekly bill came in but there were two or three put in, ‘frighted’; that is, that may well be called frightened to death. But besides those who were so frightened as to die upon the spot, there were great numbers frightened to other extremes, some frightened out of their senses, some out of their memory, and some out of their understanding.

[E]very one looked on himself and his family as in the utmost danger. [...] London might well be said to be all in tears [...]. The shrieks of women and children at the windows and doors of their houses, where their dearest relations were perhaps dying, or just dead, were so frequent to be heard as we passed the streets [...]. Tears and lamentations were seen almost in every house, especially in the first part of the visitation; for towards the latter end men’s hearts were hardened, and death was so always before their eyes, that they did not so much concern themselves for the loss of their friends, expecting that themselves should be summoned the next hour.’

Defoe was 5 in 1665: his exhaustive account resonates today, albeit as fiction.

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