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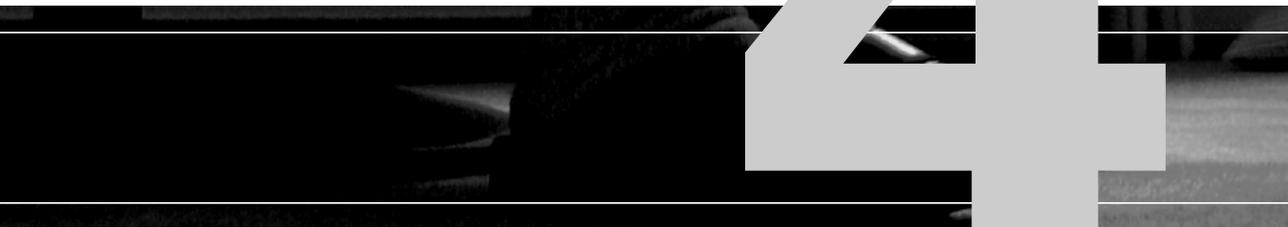
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Comorbidity in older adults with Posttraumatic Stress Disorder

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Abstract

Objective No information exists on psychiatric comorbidity in older subjects with PTSD. It is therefore unknown which factors cause comorbidity. Taken to extremes there are two possibilities: either comorbidity is caused by severity of PTSD (severity hypothesis) or it is caused by different risk factors (specificity hypothesis). This study was designed to determine which possibility comes true. The frequencies of comorbid Major Depressive Disorder and other anxiety disorders in a gradient line of severity of PTSD were determined and also comorbidity with depressive and anxiety symptoms was measured. Finally, associations were determined in logistic regression analysis taking several potential risk factors into account.

Methods Data were gathered in the third and fourth cycle of the Longitudinal Aging Study Amsterdam (LASA) from which 33 subjects with past year PTSD according to the CID-I, 66 subjects with subthreshold PTSD and 122 controls were interviewed for CID-I anxiety diagnoses and DIS depression diagnoses in the past year. Also, data regarding potential specific risk indicators (neuroticism, number of trauma and childhood adversities, age, gender, education, MMSE, ADL, number of chronic diseases) were collected and analysed.

Results Comorbidity was considerable and rises with symptom severity and more stringent PTSD diagnoses to almost forty percent. Only severity accounted for comorbidity in PTSD and specific risk indicators were not found.

Conclusions Comorbid past year anxiety and/or depression frequently goes along with PTSD and is associated with severity and not with distinct risk factors. Therefore depression and anxiety should not be seen as well founded comorbid diseases but the consequence of passing a severity threshold in a complex disorder. Implications for treatment may be to deal with PTSD first before concentrating on its comorbidity.

Key words: Comorbidity, Depression, Anxiety, PTSD, Elderly

Introduction

Comorbidity in posttraumatic stress has not been studied systematically in older persons, in spite of the great consequences it generally has in terms of mortality, quality of life and health care¹. Comorbid disorders generally lengthen duration of diseases and complicate treatment. Especially on comorbidity in older adults with PTSD research is lacking. Comorbidity can be considered as the consequence of the manifestation of many psychiatric conditions, with increasing complexity being a likely predictor of greater severity, disability and service utilization².

In younger adults comorbid lifetime^{3,4} and current⁵⁻⁷ mood disorders and anxiety disorders such as panic disorder⁸ and social phobia⁹ are described. In older adults respectively older adults with comorbid PTSD previous reports reveals 19% and 62% depressive symptoms^{10,11}.

It is unclear whether the subgroup of PTSD patients with a comorbid condition are qualitatively distinct from PTSD patients with a singular disorder. Consequently, uncertainty remains whether to focus on comorbid disorders in therapy or to wait for it to resolve during treatment of PTSD. We attempt to distinguish quantitative and qualitative aspects in two hypothesis and find arguments for their verification. The first one, addressing the quantitative distinction and coined as the severity hypothesis, postulates comorbidity as the result of cumulative severity of concurrent symptoms² to the effect that above a certain threshold of symptoms one is likely to meet criteria for a number of disorders. The severity hypothesis is in line with the finding that severity is also a predictor of comorbidity in other anxiety disorders in the elderly¹².

The second hypothesis, addressing the qualitative distinction and referred to as the 'specificity hypothesis', considers comorbidity as the result of the occurrence of specific risk factors. This has also been described previously in depression and anxiety among elderly¹³. Specific risk factors for comorbidity that have been empirically identified in previous research are: neuroticism^{14,15}, childhood adversities^{16,17}, the number of trauma's before the emergence of PTSD¹⁸, female gender¹⁹, older age¹⁹⁻²¹, worse cognitive functioning²², low education²³, number of comorbid (somatic) diseases¹⁷ and physical limitations²⁴.

This study reports on research of PTSD and concurrent comorbidity in a representative sample of older inhabitants of the Netherlands in the Longitudinal Aging Study Amsterdam (LASA).

Research-questions are:

- 1) What is the twelve month prevalence of comorbid Major Depressive Disorder and comorbid anxiety disorders in an older population with PTSD?

- 2) Regarding the severity hypothesis: Is there a quantitative distinction between singular PTSD and PTSD with comorbidity? In other words: is there an increase of comorbidity, expressed in numbers of comorbid diagnosis and mean symptom scores, in respondents with a gradient line of severity of PTSD (e.g. no PTSD, subthreshold PTSD and PTSD) and is expression of comorbidity predicted by severity of PTSD?
- 3) Regarding the specificity hypothesis: Is there a qualitative distinction between singular PTSD and PTSD with comorbidity and can specific risk indicators be identified for comorbidity? Is expression of comorbidity predicted by specific risk indicators such as neuroticism, adverse events in childhood, number of trauma, female gender, older age, cognitive functioning, education, number of somatic diseases and physical limitations?

Methods

Sample and procedures

The Longitudinal Aging Study Amsterdam (LASA) is an ongoing study of changes in autonomy and well being with aging in the Netherlands. Full details on sampling and response are described elsewhere^{26,26}. In short, a random sample of older (55-85) persons, stratified for age and sex was drawn from the population registers in 11 municipalities in the Netherlands. The sample was used in two studies. Respondents were first interviewed for the NESTOR program Living arrangements and Social Networks of older adults (response 62,3%,²⁷. About ten months later 3107 (81.7%) of the 3805 respondents of the NESTOR-LSN study took part in the LASA baseline interview in the first LASA cycle (1992/1993). Non-response was related to age ($P < 0.001$), but not to sex. The oldest old, meaning people 85 years and older, were more often found to be too ill or cognitively impaired to participate. The LASA sample was interviewed every three years. The present study was part of the third and fourth cycle in 1998/1999 and 2001/2002, when PTSD was diagnosed and an inventory of potential risk indicators took place. See figure 1.

A subgroup was selected for diagnostic interviews in a two-phase sampling procedure²⁸. The study group was confined to respondents who completed the Composite International Diagnostic Interview (CIDI)-version 2.1²⁹ in either the third or the fourth cycle of LASA (230 overlapped). Interviews were conducted by trained interviewers in the homes of respondents. For the analysis of associations 3 groups were selected in each cycle, namely those with a twelve month prevalence of PTSD according to the CIDI, a random selection of screen-positives (subthreshold PTSD) and a random selection of

screen-negatives. The results of the two cycles could be taken together in order to fortify statistical power because no overlap in respondents with PTSD-diagnoses existed and exactly the same procedures were followed in both cycles. The group with PTSD diagnosis contained 21 respondents of the third cycle and 12 respondents of the fourth cycle. Power considerations led to size the groups in the ratio 1: 2: 4³⁰.

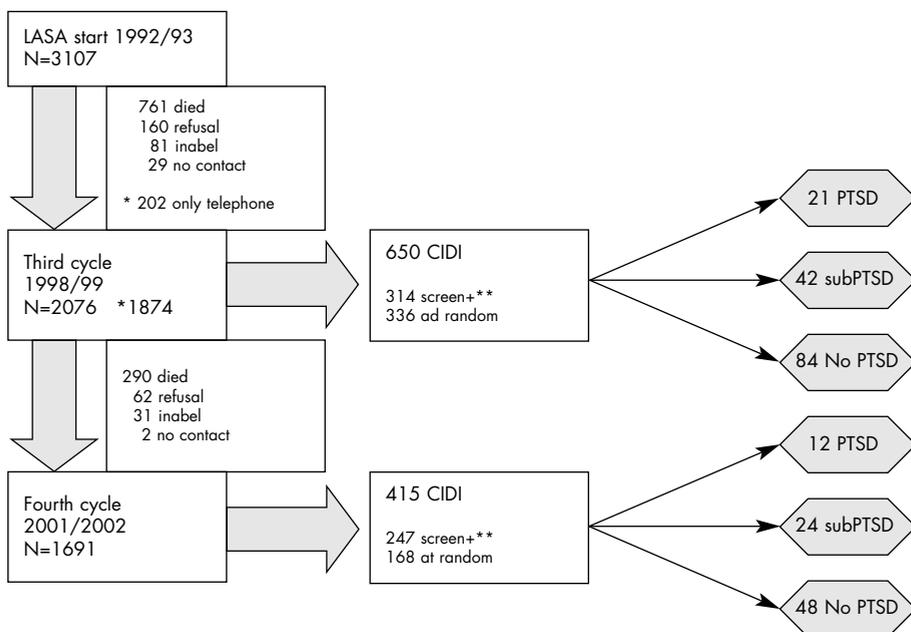


Figure 1. Collection of respondents with PTSD

* only telephone interviews precluded screening of PTSD (n=202)

** PTSD screen positive (153)and/ or depression screen positive (256); 95 overlapped

*** PTSD screen positive (188) and/or depression screen positive (152); 93 overlapped

Measures

Different interviewers administered the screening-instruments and diagnostic interviews. Interviews were tape-recorded in order to control data quality.

Symptoms of Posttraumatic Stress Disorder were measured with the Self-Rating Inventory for Posttraumatic Stress Disorder (SRIP)³. This inventory registers symptoms of PTSD independent of the level of traumatization. The questions of the SRIP correspond to 22 items from the DSM-IV, for example: “I had the feeling that past events were happening again” or “I had recurrent unpleasant memories” or “I was easily frightened”. The answers were indicated on a 4-point-scale as ‘not at all’ (one point), ‘slightly’, ‘seriously’ or ‘extremely’ (4 points). Subthreshold PTSD was considered

present if the SRIP score was ≥ 39 and there was no DSM-IV disorder. This cut-off was chosen, as earlier research in the same sample has shown (ROC-curve) that it had the best criterion validity for PTSD³².

A diagnosis of PTSD was established using the Composite International Diagnostic Interview (CIDI)-version 2.1. In the analyses twelve month prevalence rates of PTSD were used in order to minimize recall bias. PTSD-criteria were applied strictly according to DSM-IV-rules. The only criterion that was omitted was whether participants still attended parties or social events, because this question was not considered relevant for most older people. Diagnosis of Major Depressive Disorder (MDD) was measured according the Diagnostic Interview Schedule (DIS)³³. Only if the diagnosis of depression was present in the previous year of the interview it was included as a case in order to obtain the twelve month prevalence.

The CIDI-version 2.1 was also used to diagnose twelve month prevalence rates of other anxiety disorders (e.g. Generalized Anxiety Disorder (GAD), Panic Disorder with or without agoraphobia (PD), Social Phobia (SP), and Obsessive Compulsive Disorder (OCD). Specific Phobias were considered irrelevant for analyzing in the concept of comorbidity.

In order to measure subsyndromal anxiety, symptoms were assessed separately using the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS)³⁴. Also, symptoms of depression were measured with the Centre for Epidemiologic Studies Depression scale (CES-D)³⁵. Cognitive functioning was measured with the Mini Mental State Examination (MMSE)³⁶.

Traumatic events were recorded in the CIDI-version 2.1. (They included: war experience, life threatening accident, natural disaster, deadly injury, rape, (sexually) assault, attack, taken hostage, torture, other extraordinary shocking experience).

Neuroticism was measured through the (abbreviated) sub-scales of the Dutch Personality Inventory³⁷. This self-report scale was completed after the interview and mailed by the respondent. Of the 231 respondents in de total study group 24 (9.6%) did not respond. Nonresponders were significantly older [$t(229) = 4.37; p < 0.0001$], had higher SRIP-scores [$t(229) = 2.34; p < 0.0001$] and lower MMSE scores [$t(229) = -3.82; p < 0.0001$]. Next, serious adverse events in early childhood before the age of six years were recorded in a inventory specially devised for the LASA interview including serious illness or death of a parent, serious illness of oneself, maltreatment, neglect and sexual abuse. Regarding number of diseases, seven major most common physical diseases, which were decided most relevant in an older population, were assessed in detail with a questionnaire asking for specific information regarding presence, duration, principal symptoms, complications and treatment³⁸. These were lung diseases (asthma, bronchitis and pulmonary emphysema), cardiac diseases,

atherosclerotic diseases of the abdominal aorta and the arteries of the low limbs, stroke (excluding transient ischemic attacks), diabetes mellitus, malignant neoplasms, osteoarthritis and rheumatoid arthritis. Other chronic diseases were assessed in less detail. Support for the validity of the instrument was obtained by cross-checking responses with data from the respondents' general practitioners³⁸. Responses were also cross-checked with earlier answers on the same questionnaire.

Functional limitations were measured with the OECD Questionnaire, a previously validated instrument³⁹. Three questions were measuring functional limitations best, while least affecting internal reliability of the scale (0.73)⁴⁰. These questions address the functions of getting upstairs, cutting toenails and using transportation.

Outcome factors

Comorbidity was considered present if in the previous year either the respondent met the criteria of Major Depression Disorder according to the DIS or met the criteria of the anxiety disorders GAD, PD, SP, or OCD according to the CIDI.

Risk indicators

The following risk indicators for comorbidity were taken into account: total number of traumatic events in the CIDI, severity of PTSD (measured as the sum score of the SRIP), (severity of) neuroticism, number of adverse events in childhood measured by a special device for LASA, number of chronic diseases, limitations in Activities of Daily Live (ADL), (female) gender, older age, a low score (< 24 points) on the MMSE, and (lower) education.

Statistics

To address the question regarding the twelve month prevalence (question 1): simple descriptive analyses were used.

Regarding increase of comorbidity with increase of severity of PTSD (question 2): differences in proportions of comorbidity were compared, using Chi-square test or ANOVA in three groups.

Regarding identification of specific risk indicators (question 3): risk indicators for comorbidity were evaluated with multivariate logistic regression analysis (forced entry).

Results

The study sample of the 830 respondents comprised 345 males and 490 females. Respondents from the third or fourth cycle did not differ in income, education, level of urbanization or MMSE.

With regard to the prevalences of comorbid Major Depressive Disorder and other anxiety disorders, Table 1 shows that comorbidity (defined as past year depression and/or at least one past year anxiety disorder) is about forty percent in PTSD; about twenty percent in subthreshold PTSD and declines to nearly 7 percent in controls.

Table 1. Characteristics of the three groups and associations of the three groups with comorbidity and severity of psychopathology on different instruments

	PTSD N = 33 (%)	Sub- PTSD N = 64 (%)	Controls N = 132 (%)	Statistics
Male/female	11/22	20/46	61/71	$\chi^2=5.324$; $p=0.070$
Comorbidity	13 (39.4)	13 (9.1)	9 (6.8)	
MDD	10 (30.3)	6 (9.1)	3 (2.3)	
Anxiety	3 (9.1)	7 (10.6)	6 (4.5)	
No comorbidity	20 (60.6)	53 (80.3)	123 (93.2)	$\chi^2=23.277$; $p<0.001$
	Mean (s.d.)	Mean	Mean	F; p; post hoc test¹
Age	73.9 (8.3)	75.0 (7.9)	74.5 (7.5)	n.s.
MMSE mean score	26.9 (2.0)	26.5 (2.9)	27.0 (2.8)	n.s.
Education	3.7 (2.2)	3.4 (2.0)	3.6 (2.1)	n.s.
ADL-limitations	3.0 (2.8)	2.8 (2.8)	2.0 (2.6)	n.s.
Chronic Diseases	1.8 (1.3)	1.8 (1.3)	1.4 (1.0)	3.262; $p = 0.040$; $b>c^*$
HADS-score	8.6 (5.2)	7.0 (3.8)	3.0 (3.0)	46.050; $p < 0.001$; $a>b>c$
CESD-score	21.1 (10.9)	17.2 (8.8)	9.2 (6.8)	40.340; $p < 0.001$; $a>b>c$
SRIP-score	46.0 (8.1)	47.2 (7.1)	29.7 (4.8)	227.217; $p < 0.001$; $a>c$; $b>c$
Neuroticism**	12.6 (5.6)	11.6 (5.8)	5.7 (5.2)	32.547; $p < 0.001$; $a>c$; $b>c$
Childhood events	0.9 (0.9)	0.3 (0.6)	0.3 (0.5)	16.415; $p < 0.001$; $a>b$; $a>c$
Traumatic events	3.0 (2.0)	1.3 (1.6)	1.2 (1.3)	20.452; $p < 0.001$; $a>b$; $a>c$

¹ Tukey's honestly significant difference test

*PTSD =a; subthreshold PTSD =b; controls =c.

**N = 24, 58, 123, respectively due to missing data.

Table 1 supports the severity hypothesis, showing that not only comorbidity is the highest in the group with PTSD, but also are scores on different questionnaires measuring symptoms of depression and anxiety. Respondents with subthreshold PTSD also have considerable comorbidity and scale scores which are (slightly) less than those with the full diagnosis. Comorbidity falls significantly in controls and this gradient line supports the severity hypothesis. Further, subjects with PTSD and subthreshold PTSD were similar regarding gender (e.g. more females), SRIP scores, neuroticism scores and number of chronic diseases, both being clearly different from controls. Both PTSD and subthreshold PTSD having similar SRIP scores does not detract the severity hypotheses, because both groups were distinguished by the DSM-IV-criteria, which were far more stringent for the PTSD group. The three groups didn't differ in age, MMSE scores, education, and limitations in ADL. However, the number of traumatic events and adverse events in childhood were only clearly higher for the subjects with PTSD diagnosis as compared to the other two groups. Severity of PTSD is the only relevant risk indicator of comorbidity, as can be seen in Table 2. The odds ratio's express a greater chance on comorbidity if this factor is present.

With regard to the specificity hypothesis claiming that comorbidity in PTSD is predicted by specific risk indicators it can be seen from Table 2 that apart from severity neither of the other risk indicators are significant. Therefore, the specificity hypotheses for occurrence of comorbidity is not supported by this research.

Table 2. Oddsratio's for predicting of comorbidity in PTSD

Risk factor	Comorbidity in PTSD	
	Odds ratio	CI
Age	0.6	0.3-1.5
Gender	1.0	0.4-2.5
Education	1.2	0.5-2.8
MMSE-score	0.7	0.1-3.7
Chronic Diseases	0.8	0.3-2.5
Limitations in ADL	0.7	0.3-1.7
Neuroticism	2.4	0.8-7.6
SRIP-score	4.0	1.6-10.0
Adverse events in childhood	1.6	0.7-3.9
Traumatic events	-	-

Dichotomized values: neuroticism (<5 v. 5 or more) SRIP-score (<39 v. 39 or more); adverse events in childhood (0 v. 1 or more); age (<70 v. 70 or more); MMSE score (<24 v. 24 or more); Traumatic (CID) events (<2 v. 2 or more) became a constant; Education (1 or 2 e.g. elementary education or less v. more); Number of chronic diseases (none v. 1 or more); Limitations in Activities of Daily Live (none v. 1 or more problems).

Discussion

This is the first study that describes past year comorbidity in a community based older population with past-year PTSD. Comorbidity of Major Depressive Disorders and anxiety disorders amounts to 40 percent which can be deemed considerable. The severity hypothesis is supported because more severe symptoms of PTSD goes along with an increased chance for comorbid disorders and symptoms of other disorders. It means that if a certain amount of symptoms is reached in a complex disorder as PTSD a number of other disorders can be diagnosed as well because shared domains of symptoms are covered. Severity of PTSD being a predictor of comorbidity is in line with findings in younger population^{6,41}. Because no distinct risk indicators are found for comorbidity the specificity hypothesis is not supported by the present findings. Therefore, depression and anxiety seem not to be well founded disease entities when accompanying PTSD, but merely features of the severity of this complex disorder. However, regarding the literature of risk factors, childhood adversity was reported by Levitan as an important risk factor¹⁶ concerning comorbid anxiety disorders in a non-elderly population with PTSD. This discrepancy in findings may reflect different mechanisms in the older and the younger populations. However, further research on this topic in an older population is missing. Although neuroticism is a well known risk factor for PTSD itself in younger⁴²⁻⁴⁴ and older adults^{10,19} and for comorbidity with depression⁴⁵ it just fell short of statistical significance in this study as predictor of comorbidity in PTSD. Although it can not be ruled out that the low numbers of patients in some subgroups have precluded a significant association, its importance as a risk indicator would be far less than PTSD symptom severity, which was clearly significant.

Another risk indicator we have evaluated was the number of traumatizing events. It had no significant influence on comorbidity. Although, the mean number of events was higher in the respondents with PTSD, who had also more comorbidity, the limited number of respondents with PTSD may have hampered finding a significant association. On the other hand, the fact of (merely) experiencing more events not being a predictor is in line with the findings of Breslau⁴⁶. She studied retrospectively data from the Epidemiologic Study of Younger Adults and found hazard ratio's for (comorbid) Major Depression of 2,8 for those exposed to trauma with PTSD versus the non-exposed and 1,3 (not significant) for those exposed to trauma without PTSD. This indicates that being exposed to trauma is not enough for the co-occurrence of Depression. Once PTSD has occurred after trauma the comorbidity rate grows. Our data suggest the same pattern; severity of PTSD predicts comorbidity, but number of trauma's by itself does not. The other risk indicators such as female gender and

age did not reach significance, although female gender is more frequent in more severe PTSD. Age did not predict comorbidity in this study.

Strength of the study

This was the first population based study regarding PTSD and comorbidity in older persons. Participants were attending the LASA study, which started with a random representative sample of the older population in the Netherlands and has a good participation rate and attendance. PTSD as well as comorbidity were assessed by a standardized diagnostic interview and limited to a short time frame. This ensured that only clinically relevant concurrent comorbidity was measured. In addition, clinically relevant symptoms were measured with several validated scales. A broad set of potential risk indicators for comorbidity were assessed, using standardized measurements.

Limitations The first limitation regards attrition. Analyses were carried out in the third and fourth cycle of an longitudinal study with considerable attrition of participating subjects. The principal reason for attrition in this study was death of the respondent. Once in the study relatively few participants dropped out, but due to the long period between the LASA base line and the third cycle some changes due to attrition could have occurred, potentially compromising the representativeness of the sample. Throughout the study, the oldest old and the most frail were more likely to drop out, which may lead to underestimation of the results. The second limitation regards the power of the study. The PTSD- group was small and so were the other groups which were randomly chosen in ratio proportional the PTSD group. With limited statistical power only very strong associations reach statistical significance.

Finally, regarding causality limitations inherent to the cross-sectional design of the study should be kept in mind. The risk indicators we have found should be reproduced in studies that have a longitudinal design to become proven risk factors.

Implications of the study

Although this is the first study of psychiatric comorbidity in older adults with PTSD, other studies regarding psychiatric comorbidity underline its importance regarding the rise in morbidity, complications and mortality. Frayne et al. recently reported for women veterans the excess burden of medical illness even more pronounced in comorbid PTSD than in depression alone. She actually doubted if the excess of medical morbidity previously observed in depressed women merely was due to undiagnosed comorbid PTSD²⁴. Also, in a younger hospitalized population a more adverse outcome for comorbid PTSD in depressed patients was found, stressing the importance of recognition and treatment of PTSD⁴⁷. In addition, older adults with

depression and comorbid anxiety and PTSD had more severe illness and their response to therapy was delayed compared to (only) depressed elderly. However, after intervention of multifaceted collaborative stepped care therapy their improvement after one year was comparable to cases without comorbidity⁴⁸. An implication of our findings for treatment practice in older persons with PTSD and comorbid anxiety and/or depressive disorders is to focus firstly on PTSD diagnosis and treatment and wait for the anxiety and depression symptoms to resolve with this treatment as well since they are common accompanying conditions once PTSD has evolved (severity hypothesis). Firstly concentrating on symptoms of anxiety and depression often precludes diagnosing the underlying (clouded) PTSD and several authors have warned for this effect of comorbidity^{11;23;24}. Dealing with PTSD first before concentrating on its comorbidity may also be cost effective in health care service and is most rational since we found that comorbidity is only associated with severity aspects of PTSD.

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