

# Chronic obstructive lung disease and posttraumatic stress disorder: current perspectives

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**Background:** Several studies have reported on the co-occurrence of chronic obstructive pulmonary disease (COPD) and psychiatric conditions, with the most robust evidence base demonstrating an impact of comorbid anxiety and depression on COPD-related outcomes. In recent years, research has sought to determine if there is a co-occurrence between COPD and posttraumatic stress disorder (PTSD) as well as for associations between PTSD and COPD-related outcomes. To date, there have been no published reviews summarizing this emerging literature.

**Objectives:** The primary objective of this review was to determine if there is adequate evidence to support a co-occurrence between PTSD and COPD. Secondary objectives were to: 1) determine if there are important clinical considerations regarding the impact of PTSD on COPD management, and 2) identify targeted areas for further research.

**Methods:** A structured review was performed using a systematic search strategy limited to studies in English, addressing adults, and to articles that examined: 1) the co-occurrence of COPD and PTSD and 2) the impact of PTSD on COPD-related outcomes. To be included, articles must have addressed some type of nonreversible obstructive lung pathology.

**Results:** A total of 598 articles were identified for initial review. Upon applying the inclusion and exclusion criteria, n=19 articles or abstracts addressed our stated objectives. Overall, there is inconclusive evidence to support the co-occurrence between PTSD and COPD. Studies finding a significant co-occurrence generally had inferior methods of identifying COPD; in contrast, studies that utilized more robust COPD measures (such as a physician exam) generally failed to find a relationship. Among studies that examined the impact of PTSD on COPD-related outcomes, there was more consistent evidence that PTSD affects the perception of respiratory symptom burden and management. In addition, methods for measuring an important confounder (smoking) were generally lacking.

**Conclusion:** There is inconclusive evidence to support the co-occurrence of COPD and PTSD. There was stronger evidence implicating PTSD as an important comorbidity impacting COPD management. Further research is needed to: 1) determine whether or not COPD and PTSD are likely to be comorbid, and 2) further elucidate the mechanisms connecting PTSD and COPD-related outcomes.

**Keywords:** chronic lung disease, nonproductive cough, WTC cough syndrome, posttraumatic stress disorder, Veterans

## Background

Chronic obstructive pulmonary disease (COPD) is a preventable chronic condition best characterized by measurable, nonreversible restrictions in air flow with repeated, intermittent exacerbation of symptoms generally manifested by shortness of breath, nonproductive cough, sensations of air hunger, and reduced capacity for physical activity.<sup>1</sup> It is the third leading cause of mortality in the USA, with a prevalence estimate approximately 9%–10%.<sup>2–4</sup> COPD also contributes to substantial direct and indirect costs to both patients and systems of care.<sup>1</sup>

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In many ways, the course and characteristics of posttraumatic stress disorder (PTSD) are similar to COPD. For example, PTSD is characterized by marked intermittent patterns of exacerbations of the core symptoms – intrusive thoughts, avoidance, hyperarousability, and negative cognitions. PTSD is common (estimates ranging from 1% to 32%), generally considered treatable but incurable,<sup>5–7</sup> and is associated with increased morbidity, mortality, and health care costs.<sup>8</sup>

A considerable body of research has examined the bidirectional associations between psychiatric comorbidity and COPD; efforts that have largely been limited to the conditions of anxiety and depression.<sup>9</sup> For example, a recent meta-analysis identified 22 papers encompassing a pooled population of nearly 30,000 subjects revealed important bidirectional relationships between both anxiety and/or depression on COPD co-occurrence and the impact of anxiety and/or depression on COPD outcomes. The meta-analysis reported on three key findings: 1) mortality risk in patients with COPD and depression, 2) mortality risk or COPD outcomes and anxiety exposure, and 3) COPD and depression and/or anxiety risk. Notwithstanding methodological heterogeneity, the meta-analysis reported a higher risk for mortality among patients with COPD suffering from depression (relative risk [RR] =1.83; 95% confidence interval [CI] =1.00–3.36). Similarly, the RR for mortality or worse COPD outcomes was higher among patients with COPD and anxiety (RR =1.27; 1.02–1.58). COPD severity was also associated with greater relative risk of anxiety or depression (1.69; 1.45–1.96). In conclusion, the report emphasized the importance of performing routine monitoring for anxiety or depression in patients with COPD.

In contrast to this evidence base, we were unable to locate any reviews addressing the associations between PTSD and COPD. Our interest in performing a review of this topic was primarily driven by three factors: 1) our clinical observations, 2) the individual studies that have investigated this association, and 3) a recent review article discussing plausible immune-mediated mechanisms supporting a biological framework for the association.<sup>10</sup>

Thus, in the context of the emerging evidence base outlining the associations between psychiatric comorbidity and COPD and because of the lack of a review specifically addressing PTSD, we performed this review with the following aims: 1) to provide a comprehensive review of the literature examining the co-occurrence of PTSD and COPD, and 2) to identify areas for more focused research efforts. To the best of our knowledge this is the first review article on this topic.

## Methods

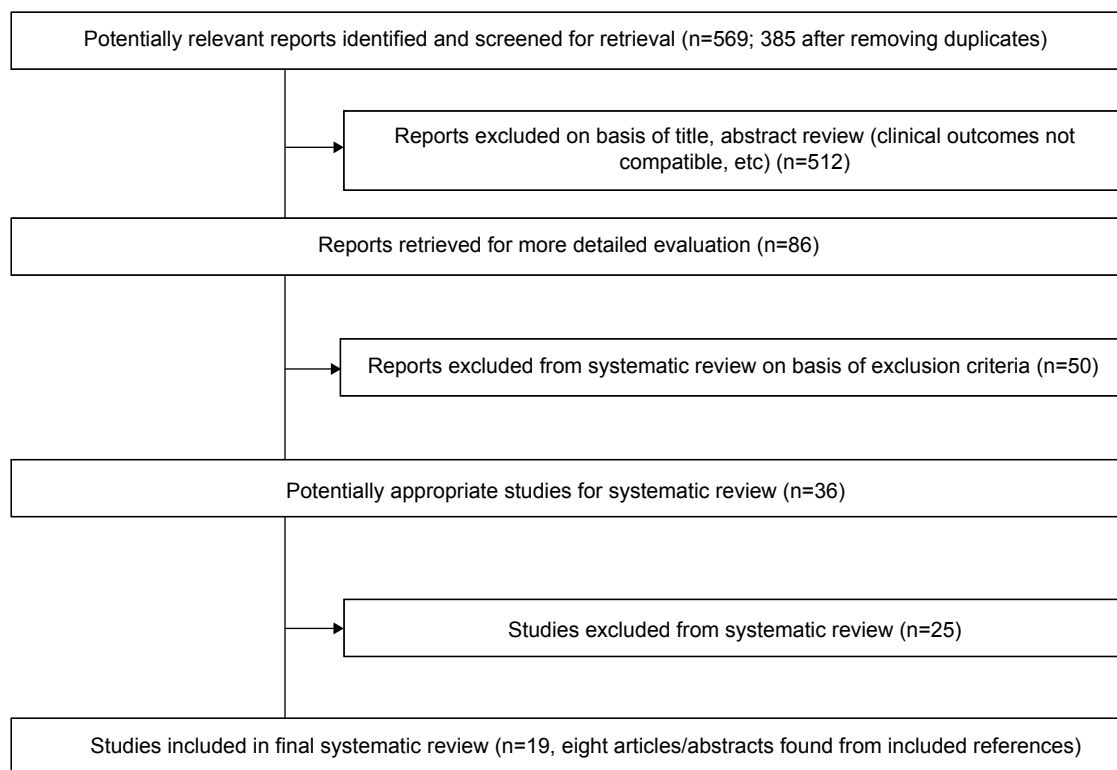
This structured review began with an initial literature search performed by a health sciences librarian (AB) using several indexed databases: MEDLINE through Ovid, Cochrane Database of Systematic Reviews through Wiley, Database of Abstracts of Reviews of Effects through Wiley, Cochrane Central Register of Controlled Trials through Wiley, Embase through Wiley, Web of Science, and [ClinicalTrials.gov](http://ClinicalTrials.gov) in January 2015. Terms included subject headings and keywords for posttraumatic stress disorder, chronic obstructive pulmonary disease, emphysema, asthma, and chronic bronchitis. No filters for language, year, etc, were applied to the searches. Full search strategies from all databases are listed in the Supplementary materials. TA reviewed the reference lists provided in each of the final selected studies to identify studies not captured in the preliminary literature search (n=8).

## Inclusion and exclusion criteria

To be included in this review, publications must have included: 1) COPD or other nonreversible obstructive lung disease states, 2) PTSD in the sample, and 3) an examination of associations between COPD and PTSD reflecting at least one of the following main topical areas: epidemiology, treatment receipt, or outcomes (eg, risk of hospitalization, and medication adherence). The review was limited to studies available in the English language. In a stepwise fashion, Figure 1 illustrates the number of articles examined and the reasons for exclusion.

Several identified studies were excluded as the focus was on the impact of PTSD on asthma or on self-reported symptoms of shortness of breath rather than COPD. We also excluded several studies examining the impact of trauma on pulmonary diseases in children. Several studies with a primary focus on the relationship between PTSD and more broadly defined medical comorbidities were also identified. In some of these studies, the methods for identifying COPD captured all respiratory illnesses; eg, cases of asthma were included with the COPD definition, or other bronchial asthma or chronic bronchitis. We elected to include these reports.<sup>11–14</sup> In at least one other case, a study examined associations between PTSD and respiratory diseases (including COPD); however, the authors only reported broad associations between the degree of medical comorbidity and PTSD and not the specific relationship between the respiratory conditions and PTSD. Consequently, this article was excluded.<sup>15</sup>

Furthermore, we identified several manuscripts focused on first responders for the events following 9/11. From this literature, there was a notable emphasis on first responders' exposure to high concentrations of air particulate matter and



**Figure 1** Flow diagram displaying the study selection process.

subsequent development of lower respiratory airway symptoms corresponding with trauma exposure and/or probable PTSD. Many of these studies evaluated exposure to the World Trade Center (WTC) dust cloud according to various factors: self-reported degree of exposure, type of first responder, and the timing of arrival to the recovery scene. Therefore, even if the studies did not specifically identify COPD per se, we included this literature in the review. Our reasoning for including this population is due to the fact that the clinical description of the lower respiratory symptoms reported by responders in the WTC recovery effort reflects many of the same symptoms of COPD. For example, official description of the symptoms related to the WTC recovery effort has been characterized by Niles et al

WTC cough syndrome is a descriptive term and requires at least one symptom in each of the three categories (upper respiratory, lower respiratory, and gastroesophageal reflux disease (p 1147)).<sup>16</sup>

The similarities between the WTC cough syndrome and COPD include measurable obstructive airflow limitations, an intermittent pattern of exacerbations of nonproductive cough, and shortness of breath. Because we thought that these studies could potentially help to shed light on the associations between PTSD and COPD, we decided to include them in the review.

## Results

From an initial pool of 598 articles, we identified 19 articles for final review. Eight articles were identified by hand searching the references for eleven of the articles identified by the literature review strategy. We found notable heterogeneity between the final studies included in the review and thus have organized the results according to the key methodological characteristics including population, methods for identifying the obstructive lung pathology, including obstructive lung pathology, COPD, and PTSD, and the primary and secondary outcomes. A focused summary containing the key elements for each of the articles is provided in Tables 1 and 2.

### Studies examining for the co-occurrence between obstructive lung disease, COPD, and PTSD

We initially focused on studies that utilized methods to separate the diagnosis of COPD from respiratory illnesses more broadly. Within this group of studies, important differences in sample characteristics were observed. Six studies focused on Veteran samples.<sup>11,13,17–20</sup> The others included community-dwelling adults, samples of patients attending outpatient clinics, and samples of patients enrolled in health organizations.<sup>12,14,21–28</sup>

**Table 1** Selected studies included in the systematic review examining for an association between PTSD and COPD and the impact of PTSD on COPD related outcomes

Study	Population and sample size	Design/data source	PTSD definition or method of identification	COPD definition or method of identification	Reported associations of interest between COPD and PTSD	Summary of findings on the primary measured outcomes
Abrams et al <sup>18</sup>	Sample of Veteran patients admitted for a COPD exacerbation (n=26,591)	Retrospective cohort design Veterans Affairs (VA) administrative data	Physician diagnosis recorded in outpatient visits prior to COPD admission	Physician diagnosis of COPD coded on inpatient encounter	Hospital readmission, 30 days mortality	No difference in readmission rates for patients with PTSD (HR, 1.17; 95% CI: 0.96–1.17) or mortality (OR, 1.19; 95% CI: 0.92–1.55). Rates of PTSD among Veterans admitted for COPD exacerbation were lower than general Veteran population (5.9%)
Felker et al <sup>19</sup>	Sample of Veteran patients with COPD attending a VA medical center (n=251)	Prospective cohort design with clinical data collection	PTSD checklist (PCL); probable PTSD with a score of $\geq 50$	Physician diagnosis of PTSD	Association between moderate, severe, or very severe COPD and PTSD	No significant association between moderate, severe, and very severe COPD and PTSD. Rates of PTSD among mild or no COPD were 10% vs 12%, 11%, and 12% for moderate, severe, and very severe respectively ( $P=0.9$ )
Glaesmer et al <sup>21</sup>	Representative sample of German population (n=1,456)	Cross-sectional self-report survey	Posttraumatic diagnostic scale (PTDS) and impact of events scale	Self-report of either COPD or bronchitis	Association between self-reported diagnoses of COPD or bronchitis and either trauma exposure or PTSD diagnosis	Trauma was associated with a higher OR for either COPD or bronchitis (3.25; 95% CI: 1.84–5.76; $P<0.001$ ); however, self-report of PTSD diagnosis according to PTSD instrument did not reach significance for association with COPD (OR, 2.25; 95% CI: 0.99–4.64)
Jones et al <sup>22</sup>	Representative sample of patients with COPD attending pulmonary rehabilitation clinic (n=100)	Prospective cohort design with clinical data collection	PTDS, impact of events scale	Physician confirmed diagnosis of COPD; chronic respiratory questionnaire – self report (CRQ-SR)	Association between improvements in exercise capacity, quality of life scores, and PTSD severity symptoms	PTSD reported in 8% of sample, PTSD symptoms did not improve following the receipt of pulmonary rehabilitation; however, symptoms of anxiety and pulmonary disease burden (CRQ-SR) scores were higher for subjects with PTSD (3.78 vs 2.99; $P=0.03$ )
Kronish et al <sup>17</sup>	Veteran sample of two VA medical centers (n=724)	Prospective cohort design with clinical data collection	Clinician administered PTSD scale	Self-report questionnaire for COPD	Association between PTSD and COPD self-report, impact of PTSD on medication adherence	COPD was reported more often in veterans with PTSD than without PTSD (22.7 vs 16.3; $P=0.03$ ). PTSD was associated with the decision to skip medications (OR, 1.95; 95% CI: 1.31–2.91; $P=0.001$ )

Trivedi et al <sup>23</sup>	Single medical center sample of COPD clinic patients (n=77)	Observational cohort design with medical records data collection	Clinician recorded PTSD diagnosis	Clinician recorded COPD diagnosis	Associations between having preexisting psychiatric illness and FEV <sub>1</sub> levels receiving home oxygen therapy	Preexisting psychiatric illness (including PTSD) was associated with lower FEV <sub>1</sub> levels receiving oxygen (P=0.049)
Sareen et al <sup>24</sup>	Large population survey, the Canadian Community Health Survey, (n=36,984)	Cross-sectional survey of community representative sample	Report of a physician diagnosis of PTSD	Report of a physician diagnosed condition of chronic bronchitis, emphysema, or COPD	Association between PTSD and obstructive pulmonary disease adjusting for demographics, other mental health comorbidity	3.8% of the sample without PTSD reported obstructive pulmonary disease vs 17.3% with PTSD; adjusted OR was 3.08 95% CI: 2.01–4.72; P<0.001. Samples reporting PTSD had lower scores on psychological well-being (OR, 2.11), past 1 year suicide attempt (OR, 2.35), and worse distress (OR, 2.66) and more days of mental health disability (OR, 2.72)
Seng et al <sup>12</sup>	Public health insurance database of adult females in Michigan, (n=17,081)	Case-control design of Medicaid program identifying 2,133 cases of PTSD matched to 14,948 without PTSD diagnosis	Administrative data code for PTSD (309.81)	Administrative data code for respiratory system illness	Associations between PTSD diagnosis, PTSD diagnosis with depression, or complex PTSD (PTSD + personality disorder) and respiratory system condition; regression models adjusting for comorbid mental health conditions	OR for respiratory system condition with any one of the PTSD conditions ranged from 3.0 to 5.1; P<0.002 after Bonferroni multiple comparison correction
Spitzer et al <sup>14</sup>	Population based health examination of German community sample, (n=3,171)	Cross-sectional survey design	PTSD determined by Structured Clinical Interview for DSM-IV. (SCID)	Computer assisted personal interview, survey questions asked about illnesses of chronic bronchitis or bronchial asthma	Logistic regression analyses examining the relationship between medical illness and PTSD controlling for clinical and demographics. Determined relationship between trauma exposure and medical illness as well	Among individuals experiencing trauma, 5.7% and 3.5% reported bronchitis or asthma respectively vs 3.8% and 1.9% without trauma Adjusted OR, 1.3 and 1.2 respectively each significant at P<0.001. For patients with PTSD, rates of bronchitis were 21.0 and for asthma 11.3; OR, 3.0 and 2.9; P<0.05 for both

(Continued)

Table 1 (Continued)

Study	Population and sample size	Design/data source	PTSD definition or method of identification	COPD definition or method of identification	Reported associations of interest between COPD and PTSD	Summary of findings on the primary measured outcomes
Spitzer et al <sup>26</sup>	Same as 2009 study restricting sample to n=1,772 with spirometry	Cross-sectional survey design	PTSD determined by Structured Clinical Interview for DSM-IV. (SCID)	Computer assisted personal interview, physician exams and pulmonary function tests, FVC, FEV <sub>1</sub> , and % predicted	Logistic regression analyses examining the relationship between pulmonary function and trauma exposure and PTSD controlling for clinical and demographic characteristics	Many significant associations between PTSD and a number of respiratory symptoms (OR ranging from 2.6 for chronic bronchitis to 8.8 for asthma attack). FVC, FEV <sub>1</sub> , and % predicted were each lower for PTSD group. P<0.01
Boscarino <sup>20</sup>	Registry of Vietnam era Veterans, Veterans experience study (n=1,399)	Cross-sectional design analyses performed on a cohort of Vietnam Era Veterans 20 years postservice	PTSD determined using the Diagnostic Interview Schedule (DIS)	Physician diagnosis of respiratory illnesses included asthma and obstructive lung diseases confirmed by medical records review (ICD-9CM codes 480–486, 490–496)	Associations between PTSD and respiratory illnesses per medical records	Unadjusted OR, 2.00, 95% CI: 1.38–2.90. Adjusted OR, 1.54, P=0.042
Schnurr et al <sup>11</sup>	Registry of Veterans, Normative Aging Study, (n=2,280)	Observational cohort design	Mississippi combat rating scale, score of >89 indicating PTSD	Physician diagnosis of either asthma or emphysema on exam completed every 3–5 years (ICD-8 codes 490–493)	Hazard ratio (HR) for associations between PTSD and either asthma or emphysema. Impact of medical comorbidity and PTSD on HR for cumulative survival	Unadjusted HR, 1.05; 95% CI: 0.89–1.22; adjusted HR, 0.95; 95% CI: 0.80–1.13. HR for pulmonary condition on cumulative survival in models including PTSD =1.22; P<0.05
Spiro et al <sup>13</sup>	Veterans Health Survey of outpatient members attending four VA clinics (n=2,262*)	Cross-sectional survey design	PTSD checklist – Civilian version meeting criteria by symptom cluster criteria	Self-report of chronic lung disease	Associations between PTSD and chronic lung disease	18.4% of veterans with PTSD had CLD vs 12.7% without PTSD; adjusted OR, 1.67, 95% CI: 1.24–2.24

Weisberg et al <sup>25</sup>	Primary care sample of patients from multiple (15) clinics located in northeast USA.	Prospective cohort design with clinical data collection	Structured clinical interview for DSM-IV indicating PTSD	Self-report of lung disease (asthma separate diagnosis)	Association with lifetime report of lung disease with clinician diagnosis of PTSD	Strong association between self-reported lung disease (not asthma) and PTSD; Cochran–Mantel–Haenszel $\chi^2$ test = 11.86; $P < 0.001$
Laurin et al <sup>27</sup>	Pulmonary clinic sample of patients from single site (n=116)	Prospective cohort design with clinical data collection	Structured psychiatric interview using the Anxiety Disorders	COPD confirmed by physician referral to clinic	Association between PTSD and COPD by sex	No significant association was found limited by only one case of PTSD was verified by psychiatric interview
Yellowlees et al <sup>28</sup>	Sample of patients admitted to a respiratory unit at a single site (n=50)	Prospective cohort design with clinical data collection	Psychiatric interview	COPD confirmed by physician referral to respiratory unit	Association between PTSD and COPD	Only one case of PTSD was identified

Note: \* $P > 0.05$ .

Abbreviations: PTSD, posttraumatic stress disorder; COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 second; CI, confidence interval; OR, odds ratio; HR, hazard ratio; CLD, chronic lung disease.

## Studies of Veterans examining for the co-occurrence of respiratory conditions, COPD and PTSD

These Veteran-based studies provided mixed evidence to support the co-occurrence between COPD and PTSD. Two studies<sup>17,19</sup> used a prospective study design with samples of Veterans recruited from outpatient clinics and tested for the co-occurrence between COPD and PTSD, but reported conflicting results. Kronish et al<sup>17</sup> investigated the impact of PTSD on medication adherence and reported a co-occurrence between COPD and PTSD. Felker et al<sup>19</sup> aimed to determine the impact of depression and anxiety on health-related quality of life among a sample of Veterans attending Veterans Health Administration outpatient clinics with at least moderate COPD, as measured by physician exam. In this study, Felker et al<sup>19</sup> utilized a self-report PTSD assessment. Thus, the lack of structured illness assessments for both PTSD and COPD in both studies may have contributed to the disparate findings.

Another study examined the impact of PTSD on rates of hospital readmission and mortality among a group of Veterans admitted for an exacerbation of COPD using Veterans Health Administration medical records data.<sup>18</sup> Although there were no direct tests for the significant co-occurrence of COPD and PTSD, the observed rates of PTSD (5.9%) were considerably lower than those observed in the general Veteran population,<sup>29</sup> suggesting a nonsignificant co-occurrence with COPD.

Three other studies among Veterans focused on the association between PTSD symptoms and respiratory illnesses more broadly. Schnurr et al<sup>11</sup> examined a longitudinal cohort of Veterans with the primary objective of exploring the relationship between PTSD symptoms and the risk for developing a pulmonary condition and cumulative survival. The pulmonary conditions included both reversible and non-reversible obstructive pulmonary disease types. The burden of PTSD symptoms was not associated with an increased risk for the development of any of the included respiratory illnesses following adjustment for baseline smoking, alcohol, and body mass index. However, a subanalysis on the mediation effect of combat exposure and PTSD symptom burden on the risk of developing a respiratory illness revealed a significant hazard ratio (HR) of 1.22 ( $P < 0.05$ ). Using a similar approach, Boscarino<sup>20</sup> analyzed a registry of Vietnam era Veterans with the primary objective of determining the relationship between PTSD and medical comorbidities. Clinical exams were used to determine all key variables, the respiratory conditions (including emphysema and asthma),

**Table 2** Studies examining the special population of first responders for the events of 9/11

Study	Population and sample size	Design/data source	PTSD definition or method of identification	COPD definition or method of identification	Reported associations of interest between COPD and PTSD	Summary of findings on the primary measured outcomes
Luft et al <sup>11</sup>	The World Trade Center Medical Monitoring and Treatment Program (WTC-MMTP) (n=8,508 police and n=12,333 non-traditional first responders)	Clinical data registry reflecting the care given by seven clinics in New York and New Jersey to qualified responders who participated in the WTC recovery effort	PTSD checklist (PCL); probable PTSD with a score of $\geq 50$	Respiratory symptoms were assessed by self-report and FEV <sub>1</sub> measured using spirometry	Rates of probable PTSD, respiratory symptoms, and abnormal FEV <sub>1</sub> ; Structural equation models evaluated for the relationship between probable PTSD and abnormal FEV <sub>1</sub> or lower respiratory symptoms ( $\geq 1$ )	Rates of probable PTSD differed by responder type; police 5.9% vs nontraditional responders 23.0%; $P < 0.001$ . Odds ratio for PTSD and respiratory symptoms was 1.4, 95% CI: 1.2–1.8 for police; whereas for non-traditional responders, OR, 1.2, 95% CI: 1.1–1.4 up to 2.0, 95% CI: 1.8–2.2; variable according to degree of dust cloud exposure and hours worked. Structural equation models showed correlation between probable PTSD and abnormal FEV <sub>1</sub> and respiratory symptoms; $P < 0.05$
Niles et al <sup>16</sup>	WTC-MMTP for the FDNY (n=5,363)	Clinical data registry reflecting FDNY firefighters reporting to WTC event within first 2 weeks of 9/11	PCL with probable PTSD with a score of $\geq 50$	WTC cough syndrome	Rates of baseline probable PTSD, follow-up probable PTSD; PTSD score increase, and WTC cough syndrome, FEV <sub>1</sub> % predicted, logistic regression models adjusting for demographics	Baseline WTC cough syndrome was associated with baseline probable PTSD OR, 3.59, 95% CI: 2.93–4.39; Follow up probable PTSD and PTSD score increase each were significantly associated with WTC cough syndrome at follow up and the delayed onset of the cough syndrome with all OR ranging from 1.78 to 2.14; and none of the 95% CI crossing 1. Baseline probable PTSD was not associated with abnormal baseline FEV <sub>1</sub> % predicted
Webber et al <sup>12</sup>	WTC-MMTP for the FDNY (n=10,943)	Clinical data registry reflecting FDNY firefighters reporting to WTC event within first 2 weeks of 9/11	PCL-civilian version; probable PTSD with a score of $\geq 44$	Obstructive Airway Disease (OAD), defined as at least three physician documented visits done every 12–18 months with either asthma, chronic bronchitis, COPD/ emphysema or sinusitis	Association between WTC dust cloud exposure determined by arrival timing, first responder type (firefighter, EMS) and OAD; association between PTSD and OAD	41.8% with probable PTSD or depression self-reported an OAD diagnosis; total sample rates of OAD = 15.5%. No statistical test for significance was reported. 33.3% with either probable PTSD or depression reported OAD

**Abbreviations:** EMS, emergency medical service; FEV<sub>1</sub>, forced expiratory volume in 1 second; FDNY, Fire Department of the City of New York; CI, confidence interval; OR, odds ratio; PTSD, posttraumatic stress disorder.



and PTSD. Boscarino<sup>20</sup> found that PTSD increased the risk of having a respiratory condition which remained significant after adjustment for up to 14 control variables including demographics, drug use, alcohol abuse, tobacco use, army enlistment status, and baseline enlistment physical and psychiatric status. While each of these studies utilized longitudinal registries and similar PTSD and pulmonary condition identification methods, a strength of the Boscarino study<sup>20</sup> was the inclusion of a large number of PTSD cases relative to the study by Schnurr et al<sup>11</sup> (n=332 vs n=6). The Schnurr study<sup>11</sup> overcame limitations of statistical power by examining PTSD symptom burden as a continuous variable.

The final Veteran-based study was performed by Spiro et al<sup>13</sup> who examined an ambulatory sample of Veterans accessing outpatient services. The study was conducted to address prior studies' conflicting results regarding associations between PTSD and health status using medical claims based data. The authors reasoned that a study design using self-reported illness measures would be a better representation of health status relative to coded medical data.<sup>13</sup> As with the aforementioned studies, the authors characterized the pulmonary conditions as chronic lung disease and did not distinguish COPD from related respiratory disorders. The study found higher rates of chronic lung disease among a sample of Vietnam Veterans with PTSD relative to those without PTSD.

We conclude that, among studies focused on Veterans testing for the co-occurrence of respiratory conditions or COPD, and PTSD, there is insufficient evidence to support a clear relationship. While several studies identified a significant co-occurrence between PTSD and COPD, only one study had the primary objective of determining the presence of a significant co-occurrence between COPD severity and PTSD.<sup>19</sup> Also, while older studies benefitted from a more robust method of determining PTSD, these studies lacked the ability to distinguish COPD from other respiratory conditions more broadly. This methodological heterogeneity likely accounted for the disparate findings across studies.

## Studies of clinic and community samples examining for the co-occurrence of respiratory conditions, COPD and PTSD

A second set of studies was identified that focused on non-Veteran samples. From this group, ten studies examined community-dwelling adults, clinical samples, or health system enrollees.<sup>12,14,21-28</sup> As with the Veteran-based literature, there was inconclusive evidence to support a clear co-occurrence of PTSD and COPD. Glaesmer et al<sup>21</sup> examined

for the co-occurrence between PTSD and trauma exposure with several medical conditions, including COPD, within a sample of German community members. Four hundred twenty-three subjects (29.1%) reported trauma exposure with 67 (4.6%) classified as having PTSD based on a validated clinician-administered scale. All medical conditions were determined using self-report. The authors found an association between either COPD or chronic bronchitis and trauma exposure. However, when the sample was restricted to those with PTSD based on responses to a validated symptom scale,<sup>21</sup> the association was no longer statistically significant. As with the Schnurr et al report,<sup>11</sup> the relatively low numbers of cases of PTSD may have contributed to the absence of a statistically significant association.

Jones et al<sup>22</sup> examined the prevalence of PTSD among patients with COPD attending a pulmonary rehabilitation program. Health status was assessed by self-report, while PTSD was measured using the Posttraumatic Diagnostic Scale. As the prevalence of PTSD in the study sample (8%) is similar to the prevalence of PTSD observed in the general population this suggests the lack of a relationship with COPD,<sup>22</sup> although again, it is unlikely that the study had adequate statistical power to detect an association if one existed. The remaining three studies either identified PTSD too infrequently (eg, <5 cases) for meaningful analysis or did not distinguish PTSD from other psychiatric conditions.<sup>23,27,28</sup>

The remaining five studies are discussed individually, primarily because each of the study methods relied on a broader definition of respiratory illness that also included COPD.<sup>12,14,24-26</sup> Sareen et al<sup>24</sup> examined associations between PTSD and respiratory disease in a sample of nearly 37,000 community members. COPD, chronic bronchitis, and emphysema were combined into a composite measure of respiratory conditions. Each condition, as well as PTSD, was determined according to whether the respondents had ever been diagnosed with the condition by a physician.<sup>24</sup> Despite the relatively low rate of PTSD (ie, 1%, n=478), individuals with PTSD reported a fourfold increase in the odds of obstructive lung conditions relative to those without PTSD.

In a series of two smaller, similarly designed studies on a representative sample of community-dwelling adults in Germany, Spitzer et al<sup>14,26</sup> report a significant co-occurrence between obstructive respiratory conditions and PTSD. The initial study identified PTSD based on a clinical exam, while the respiratory conditions were determined by a computer-assisted telephone survey. PTSD, which was identified in 62 subjects (2%), was associated with a threefold increase in reporting one of the respiratory conditions. The follow-up

study utilized the same cohort and augmented the analyses by using spirometry to define the degree of pulmonary dysfunction. The authors reported a positive relationship between PTSD and the percent predicted forced expiratory volume spirometry abnormalities. The authors performed additional examinations on the mediation effect of trauma exposure and PTSD on the spirometry findings. After including trauma in the models, the association between PTSD and abnormal spirometry no longer retained significance. As noted in the review by Douwes et al<sup>30</sup> factors which may have contributed to this inconsistency included the low rate of PTSD in the sample (n=28/1%) as well as the clinical and demographic differences between the subjects with and without PTSD.

Among studies examining community-dwelling samples, there appears to be some evidence of a significant co-occurrence between PTSD and obstructive lung disease more broadly. However, this may not be representative of obstructive lung disease or specifically COPD, particularly when more definitive measures are used (eg, spirometry). In a study involving a clinical sample of primary care patients, Weisberg et al<sup>25</sup> examined the relationship between PTSD and somatic complaints. Consistent with findings from treatment-seeking populations, PTSD was found in 37% of the sample. A significant co-occurrence between PTSD and self-reported lung disease was reported. As with several prior studies described above, details regarding how many of these cases actually represented COPD were not discussed.<sup>25</sup>

Finally, one study was identified that used administrative data to examine patterns of medical comorbidity associated with PTSD. Using medical encounter diagnostic codes to identify PTSD and respiratory system illnesses, the authors reported a 4-year period prevalence of PTSD of 14.3% and a 4-year period prevalence of respiratory system conditions of 51%. The odds of having a respiratory condition based on the presence (vs absence) of PTSD ranged from threefold to sixfold higher depending on comorbid depression.<sup>12</sup>

In summarizing this particular group of studies, we found inconclusive evidence to support the significant co-occurrence between COPD and PTSD. While some studies report a substantive co-occurrence of PTSD and respiratory illnesses, these reports tend to suffer from an inability to distinguish COPD from respiratory illnesses more broadly. Based on the evidence reviewed above, it is difficult to draw firm conclusions due to the heterogeneity of the published methods, small numbers of cases of PTSD, and the lack of sufficient diagnostic procedures for definitively identifying COPD. Acknowledging the robust evidence base<sup>30</sup> between anxiety conditions and asthma, one could conclude that

the studies reporting a significant co-occurrence using nonspecific respiratory illness methods (eg, ICD-9 codes for all respiratory conditions) were much more likely to have identified samples predominantly suffering from asthma.

## Associations between lower respiratory symptoms and PTSD among WTC survivors

This review revealed a relevant group of studies (n=3) that examined the impact of the events of September 11, 2001. This historic event resulted in a mass population exposure to a traumatic event coupled with a dust cloud characterizing a severe single exposure to a lung irritant. For many community dwellers living in close proximity to the WTC and for first responders, this dust cloud exposure has been linked to a COPD-like illness that has been further classified as WTC cough syndrome. This syndrome shares many specific signs and symptoms with COPD (eg, nonproductive cough, shortness of breath, obstructive spirometry pattern).<sup>16,31,32</sup> Among the studies that assessed for PTSD, there were strong positive associations with WTC cough syndrome (further summarized in Table 2). It is important to note, however, the WTC cough syndrome that has emerged largely represents airway dysfunction from one pinpoint exposure to the dust cloud and is likely not representative of the average experience with COPD.

## Associations between PTSD and obstructive lung disease outcomes

Several studies reported COPD-related outcomes in relation to PTSD. Outcomes examined included medication adherence, hospital readmission, mortality, COPD severity, quality of life, and response to cardiopulmonary exercise therapy. In our previous study of Veterans with a COPD-related admission, there was a slight but nonsignificant trend toward a positive relationship between PTSD and mortality (odds ratio [OR], 1.19; 0.92–1.55) or readmission (HR, 1.16; 0.96–1.42).<sup>18</sup> Other studies provided evidence for PTSD negatively impacting other important outcomes. For example, Jones et al<sup>22</sup> reported worse COPD illness burden (measured by the chronic respiratory questionnaire – self report) among patients with PTSD and a lack of response to cardiopulmonary therapy.<sup>22</sup> In addition, patients with PTSD have been found to be more likely to skip medications<sup>17</sup> and are subject to delays in the delivery of oxygen therapy.<sup>23</sup> The finding that PTSD adversely affects adherence was also reported in another study by Kronish et al<sup>33</sup> and has been replicated in other populations.<sup>34–36</sup> The evidence from this literature

base indicates that nonadherence to medications for medical problems is associated with PTSD, acting independent to other mental health conditions. This evidence has important implications for medical outcomes.<sup>17</sup> Therefore, it is feasible that poor adherence to COPD treatment contributes to the worse outcomes observed among those with PTSD.

In summary, there is some evidence that PTSD plays a role in the perception of COPD illness burden and subsequent illness management goals (eg, adherence) and treatment response rates. In part, this relationship may well be mediated by tobacco as it is established that individuals suffering from PTSD have higher rates of tobacco abuse.<sup>37–39</sup> Unfortunately, in our review of the methods used to capture tobacco use we found a high degree of variability which limited our ability to infer the degree by which tobacco mediated the impact of PTSD on COPD outcomes.

## Implications of comorbid COPD and PTSD

As the population ages, COPD prevalence is likely to increase, emphasizing the need for health care systems to recognize patterns of comorbidity associated with COPD. Although there is no firm evidence to support the co-occurrence of COPD and PTSD per se, the evidence supports conclusions that when the two chronic conditions are comorbid, there are important considerations for management. The inconsistencies observed in this review of the literature may be due, in part, to methodological heterogeneity as reflected by differences in case identification, symptom measurement, and sample characteristics. This observation supports the need for more research in this area. However, we do acknowledge that prior research suggests that individuals with anxiety and depressive conditions perceive a greater respiratory symptom burden relative to controls.<sup>40</sup>

Irrespective of the mixed research findings, it is important that clinicians recognize that evolving medical illnesses represent a point of vulnerability within the mental health of aging adults. It is therefore incumbent upon clinicians to utilize adequate mental health screening approaches to identify anxiety, depression, and trauma exposures until future studies can more definitively address the extant methodological limitations outlined by this review.

## Disclosure

The views reflected in this report are those of the authors and do not necessarily reflect the opinions of the Department of Veterans Affairs. The authors report no conflicts of interest in this work.

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## Supplementary materials Ovid MEDLINE(R) in-process and other non-indexed citations and Ovid MEDLINE(R) 1946 to present (run on January 2, 2015, 103 results)

1. exp Stress Disorders, Post-Traumatic/
2. (PTSD or Posttraumatic Neuroses or Post traumatic Neuroses or Post-traumatic Neuroses or Posttraumatic Stress Disorder\* or Post traumatic Stress Disorder\*).tw
3. exp Combat Disorders/
4. (Combat Disorder\* or Combat Neurosis or Combat Neuroses or War Neurosis or War Neuroses or Shell Shock\* or Combat Stress Disorder\*).tw
5. 1 or 2 or 3 or 4
6. exp Pulmonary Disease, Chronic Obstructive/
7. exp asthma/
8. (COPD or Chronic Obstructive Pulmonary Disease or COAD or Chronic Obstructive Airway Disease or Chronic Obstructive Lung Disease or Chronic Airflow Obstruction\* or Chronic Bronchitis or Emphysema\* or Asthma\*).tw
9. 6 or 7 or 8
10. 5 and 9

## CINAHL via EBSCO (Run on January 6, 2015, 42 Results)

1. (MH "Stress Disorders, Post-Traumatic+")
2. PTSD or "Posttraumatic Neuroses" or "Post traumatic Neuroses" or "Post-traumatic Neuroses" or "Post-traumatic Stress Disorder\*" or "Post traumatic Stress Disorder\*"
3. "Combat Disorder\*" or "Combat Neurosis" or "Combat Neuroses" or "War Neurosis" or "War Neuroses" or "Shell Shock\*" or "Combat Stress Disorder\*"
4. S1 OR S2 OR S3
5. (MH "Pulmonary Disease, Chronic Obstructive+")
6. (MH "Asthma+")
7. (MH "Emphysema")
8. COPD or "Chronic Obstructive Pulmonary Disease" or COAD or "Chronic Obstructive Airway Disease" or "Chronic Obstructive Lung Disease" or "Chronic Airflow Obstruction\*" or "Chronic Bronchitis" or Emphysema\* or Asthma\*
9. S5 OR S6 OR S7 OR S8
10. S4 AND S9

## Cochrane Library via Wiley (Searched on January 6, 2015, Cochrane Database of Systematic Reviews, 0, Database of Abstracts of Reviews of Effects, 0, CENTRAL 6)

1. MeSH descriptor: [Stress Disorders, Post-Traumatic] explode all trees
2. PTSD or "Posttraumatic Neuroses" or "Post traumatic Neuroses" or "Post-traumatic Neuroses" or "Posttraumatic Stress Disorder\*" or "Post traumatic Stress Disorder\*":ti, ab, kw (Word variations have been searched)
3. MeSH descriptor: [Combat Disorders] explode all trees
4. "Combat Disorder\*" or "Combat Neurosis" or "Combat Neuroses" or "War Neurosis" or "War Neuroses" or "Shell Shock\*" or "Combat Stress Disorder\*":ti, ab, kw (Word variations have been searched)
5. #1 or #2 or #3
6. MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees
7. MeSH descriptor: [Asthma] explode all trees
8. COPD or "Chronic Obstructive Pulmonary Disease" or COAD or "Chronic Obstructive Airway Disease" or "Chronic Obstructive Lung Disease" or "Chronic Airflow Obstruction\*" or "Chronic Bronchitis" or Emphysema\* or Asthma\*:ti, ab, kw (Word variations have been searched)
9. #6 or #7 or #8
10. #5 and #9

## Web of Science (Searched on January 6, 2015, 114 results found)

1. PTSD or "Posttraumatic Neuroses" or "Post traumatic Neuroses" or "Post-traumatic Neuroses" or "Post-traumatic Stress Disorder\*" or "Post traumatic Stress Disorder\*"
2. "Combat Disorder\*" or "Combat Neurosis" or "Combat Neuroses" or "War Neurosis" or "War Neuroses" or "Shell Shock\*" or "Combat Stress Disorder\*"
3. 1 or 2
4. COPD or "Chronic Obstructive Pulmonary Disease" or COAD or "Chronic Obstructive Airway Disease" or "Chronic Obstructive Lung Disease" or "Chronic Airflow Obstruction\*" or "Chronic Bronchitis" or Emphysema\* or Asthma\*
5. 3 and 4

## Embase (Run on January 6, 2015, 296 results found)

1. 'posttraumatic stress disorder'/exp
2. PTSD or "Posttraumatic Neuroses" or "Post traumatic Neuroses" or "Post-traumatic Neuroses" or "Post-traumatic Stress Disorder" or "Post traumatic Stress Disorder" OR "Posttraumatic Stress Disorders" or "Post traumatic Stress Disorders"
3. "Combat Disorder" or "Combat Neurosis" or "Combat Neuroses" or "War Neurosis" or "War Neuroses" or "Shell Shock" or "Combat Stress Disorder" OR "Combat Disorders" or "Combat Neurosis" or "Combat Neuroses" or "War Neurosis" or "War Neuroses" or "Shell Shocked" or "Combat Stress Disorders"
4. #1 OR #2 OR #3
5. 'chronic obstructive lung disease'/exp
6. 'asthma'/exp
7. 'lung emphysema'/exp
8. COPD or "Chronic Obstructive Pulmonary Disease" or COAD or "Chronic Obstructive Airway Disease" or "Chronic Obstructive Lung Disease" or "Chronic Airflow Obstruction" or "Chronic Bronchitis" or Emphysema\* or Asthma\* or "Chronic Airflow Obstructions" or Emphysemas or Asthmatic OR asthmas
9. #5 Or #6 OR #7 OR #8
10. #4 AND #9

## Clinicaltrials.gov (Run on January 7, 2015, 8 results found)

### Searches

COPD OR Chronic Obstructive Pulmonary Disease OR COAD OR Chronic Obstructive Airway Disease OR Chronic Obstructive Lung Disease OR Chronic Airflow Obstruction\* OR Chronic Bronchitis OR Emphysema\* OR Asthma\*

With condition: post traumatic stress disorder

1 result

COPD OR Chronic Obstructive Pulmonary Disease OR COAD OR Chronic Obstructive Airway Disease OR Chronic Obstructive Lung Disease OR Chronic Airflow Obstruction\* OR Chronic Bronchitis OR Emphysema\* OR Asthma\*

With condition: posttraumatic

1 result found

COPD OR Chronic Obstructive Pulmonary Disease OR COAD OR Chronic Obstructive Airway Disease OR Chronic Obstructive Lung Disease OR Chronic Airflow Obstruction\* OR Chronic Bronchitis OR Emphysema\* OR Asthma\*

With condition: combat

0 results

Asthma

With condition: war

0 results

Asthma

With condition: combat

0 results

Asthma

With condition: posttraumatic

3 results

COPD

With condition: war

0 results

COPD

With condition: combat

0 results

COPD

With condition: posttraumatic

0 results

Bronchitis

With condition: war

0 results

Bronchitis

With condition: combat

0 results

Bronchitis

With condition: posttraumatic

0 results

Emphysema

With condition: war

0 results

Emphysema

With condition: combat

0 results

Emphysema

With condition: posttraumatic

0 results

Post traumatic

With condition: asthma

3 results

Post traumatic

With condition: chronic obstructive airway

0 results

Post traumatic

With condition: emphysema

0 results

Post traumatic

With condition: bronchitis

0 results

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