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Comorbid posttraumatic stress disorder and major depressive disorder are associated with asthma morbidity among World Trade Center workers

Juan P. Wisnivesky, MD, DrPH [*,†]; Steven B. Markowitz, MD, DrPH [‡]; Shynah James, MPH [*]; Kim Stone, MPH [*]; Brittany Dickens, BA [‡]; Paula Busse, MD [§]; Laura Crowley, MD [||]; Alex Federman, MD, MPH [*]; Craig Katz, MD [¶]; Adam Gonzalez, PhD [#]

[*] Division of General Internal Medicine, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York
[†] Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York
[‡] Occupational-Environmental Medicine, Queens College, City University of New York, Flushing, New York
[§] Division of Allergy and Immunology, Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, New York
[||] Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, New York
[¶] Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, New York
[#] Department of Psychiatry and Behavioral Health, Renaissance School of Medicine, Stony Brook University, Stony Brook, New York

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ABSTRACT

Background: World Trade Center (WTC) rescue and recovery workers have a high burden of asthma, comorbid posttraumatic stress disorder (PTSD), and major depressive disorder (MDD). PTSD is associated with worse asthma outcomes.

Objective: In this study, we evaluated whether the relationship between PTSD and asthma morbidity is modified by the presence of MDD.

Methods: We used data from a cohort of WTC workers with asthma. Asthma control (asthma control questionnaire), resource utilization, and quality of life (asthma quality of life questionnaire) were evaluated. We used regression analyses to evaluate the adjusted association of PTSD and MDD with asthma control, resource utilization, and quality of life.

Results: Of the study cohort of 293 WTC workers with asthma, 19% had PTSD alone, 2% had MDD alone, and 12% had PTSD and MDD. Adjusted mean differences (95% confidence interval) in asthma control questionnaire scores were 1.32 (0.85-1.80) for WTC workers with PTSD and MDD, 0.44 (0.03-0.84) for those with PTSD alone, and 0.50 (−0.38 to 1.38) for workers with MDD alone compared with those without MDD or PTSD. WTC workers with PTSD and MDD, PTSD alone, and MDD alone had mean (95% confidence interval) adjusted differences in asthma quality of life questionnaire scores of −1.67 (−2.22 to −1.12), −0.56 (−2.23 to −1.12), and −1.21 (−2.23 to −0.18), respectively, compared with workers without MDD or PTSD. Similar patterns were observed for acute resource utilization.

Conclusion: PTSD and MDD seem to have a synergistic effect that worsens asthma control and quality of life. Efforts to improve asthma outcomes in this population should address the negative impacts of these common mental health conditions.

Reprints: Juan P. Wisnivesky, MD, DrPH, Division of General Internal Medicine, Department of Medicine, Icahn School of Medicine at Mount Sinai, One Gustave Levy Place, Box 1087, New York, NY 10029; E-mail: juan.wisnivesky@mssm.edu.

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Introduction

Asthma is one of the most common chronic conditions reported among rescue and recovery workers and other populations exposed to the debris after the collapse of the World Trade Center (WTC) towers on September 11, 2001, (or ground zero) during the subsequent months.[1,2] Over a follow-up period of more than 10 years, multiple studies have reported that up to one-third of exposed individuals have developed asthma.[2-5] Research has also found that asthma is a major source of morbidity and poor quality of life among WTC-exposed populations and an important contributor to health care costs.[6-8]

Posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) are the most common mental health conditions among WTC workers.[9] Two systematic reviews of the health effects of the WTC attacks documented that workers and first responders were more than 10 times more likely to have PTSD symptoms compared with the general population.[10,11] Similarly, symptoms of MDD have been documented in up to 15% of WTC workers and exposed local residents.[12] Moreover, many WTC workers have comorbid PTSD and MDD.[12-14] PTSD is one of the strongest risk factors for the lack of asthma control, decreased asthma-related quality of life, and increased healthcare resource utilization among WTC-exposed populations.[5,15,16] Similarly, MDD (its symptoms, in particular) is a risk factor for worse asthma outcomes in the general population; however, this association has not been found in the setting of WTC exposure.[17-19] Despite the high prevalence and potential interrelationship among these mental health conditions, previous studies have not evaluated the combined impact of PTSD and MDD on asthma morbidity among WTC workers.

In this study, we used data from a well-characterized cohort of WTC workers with asthma to assess the interaction between PTSD and MDD on asthma control, asthma-related resource utilization, and quality of life.

Methods

Study Population

We recruited a cohort of WTC rescue and recovery workers with a physician diagnosis of asthma that was monitored or treated at the Mount Sinai Hospital or North Shore-Long Island Jewish Health System/Queens College sites of the World Trade Center Health Programs (WTCHP) Clinical Centers of Excellence. WTCHP-eligible general responders worked or volunteered for at least 4 hours from September 11 to 14, 2001, at least 24 hours during September 2001, or at least 80 hours from September to December 2001. Members of the Office of the Chief Medical Examiner who processed human remains and workers from the Port Authority Trans-Hudson Corporation who were engaged in cleaning tunnels for at least 24 hours from September 11, 2001 to July 1, 2002, are also eligible. Additional details about the WTCHP have been previously reported.[20,21]

Inclusion criteria included age 18 years or older, physician diagnosis of asthma, and the ability to communicate in English or Spanish. WTC workers with a history of considerable tobacco exposure ($\geq$15 pack-years of smoking history), chronic obstructive lung disease, or other chronic respiratory illnesses were excluded from the study.

Potential study participants who had already indicated their willingness to be contacted for research were mailed an invitation and later contacted by research staff. Those interested in participating signed informed consent, underwent a short screening assessment, and then completed a standardized in-person interview conducted in English or Spanish depending on the participant's preference. The study was approved by the institutional review boards of the Icahn School of Medicine at Mount Sinai and that of Queens College, City University of New York.

Study Variables

Sociodemographic information, including age, sex, race and ethnicity, education, income, marital status, and language, was ascertained using validated tools.[22] We also collected information regarding asthma history, asthma diagnosis in relation to WTC exposure, medication regimen, and family history of asthma, and level of WTC exposure.[2]

We used the Structured Clinical Interview for Diagnostic and Statistical Manual for Mental Disorders (SCID) patient edition version 5 to assess for the presence of PTSD or MDD.[23] The SCID is the reference standard for psychiatric interviews, has excellent reliability and validity, and was administered by trained study personnel. Based on the results of this assessment, participants were classified into the following 4 groups, namely: (1) no PTSD or MDD; (2) PTSD alone; (3) MDD alone; and (4) both PTSD and MDD.

Primary outcomes included asthma control, acute asthma-related resource utilization, and asthma-related quality of life. The asthma control questionnaire (ACQ) was used to assess the level of asthma control among study participants.[24] The ACQ is a well-validated tool that has been extensively used in epidemiologic studies and clinical trials to assess asthma symptoms and use of rescue medications over the previous week. The ACQ items are scored on a scale of 0 to 6, with higher scores indicating worse asthma control; the minimal clinically significant difference is 0.5 units.[25]

Resource utilization related to acute asthma exacerbations was assessed on the basis of self-reports of the number of emergency department (ER) visits or hospitalizations during the previous 12 months. We assessed the asthma-related quality of life using the mini asthma quality of life questionnaire (AQLQ). This validated 15-item tool assesses several domains of quality of life, including physical, emotional, social, and occupational limitations because of asthma in the previous 2 weeks.[26] Responses were generated on a Likert scale with higher scores indicating better quality of life.

Statistical Analysis

We used analysis of variance and the χ^2 test to compare the baseline characteristics of WTC workers according to the presence or absence of PTSD or MDD. We compared unadjusted ACQ and AQLQ scores among the 4 study groups using analysis of variance. Unadjusted rates of ER visits and hospitalizations were compared using χ^2 test.

We fitted linear regressions models to compare ACQ and AQLQ scores for the 4 PTSD and MDD groups after controlling for age, sex, race/ethnicity, education, income, asthma onset pre vs post 9/11, comorbidities, and WTC exposure. Adjusted rates of asthma-related resource utilization in the previous year were compared using logistic regression. We computed odds ratios and 95% confidence intervals (CI) for acute health care utilization, using the group of workers without PTSD or MDD as a reference group. Analyses were performed using Statistical Analysis System version 9.4 (SAS Institute, Inc, Cary, North Carolina) statistical software, using 2-sided *P* values.

Results

Between February 2017 and January 2020, we identified 130 individuals that were contacted and found ineligible during screening (23% reported no history of asthma, 23% had a history of chronic obstructive pulmonary disease, 14% were non-English or Spanish speakers, and 39% owing to other reasons) and enrolled 307 eligible participants. Of these 307 WTC workers, 3 were found to be ineligible after enrollment, and 11 dropped out after

recruitment. Thus, our final cohort included 293 WTC workers with asthma. Overall, 19% of the study participants had PTSD alone, 2% had MDD alone, and 12% had PTSD and MDD. Baseline characteristics of study participants without PTSD or MDD, with PTSD alone, MDD alone or PTSD and MDD are illustrated in Table 1. WTC workers with PTSD and MDD or PTSD alone were more likely to be Hispanic ($P = .01$) and have a lower income ($P = .01$) than those without PTSD or MDD. The percentage of patients with asthma onset after exposure to the WTC site was 90% for workers with PTSD and MDD, 85% for those with PTSD alone, 67% for those with MDD alone, and 82% for workers without PTSD or MDD ($P = .40$). No significant differences in other baseline characteristics were observed among the 4 study groups ($P > .05$).

Mean (±SD) ACQ scores were 2.35 (±1.12) for WTC workers with PTSD and MDD, 1.71 (±1.10) for workers with PTSD alone, 1.61 (±1.09) for workers with MDD alone, and 1.19 (±1.01) for workers with neither PTSD nor MDD (Table 2). Compared with workers without PTSD and MDD, the unadjusted mean difference (95% CI) in ACQ scores were 1.16 (0.76-1.55) for WTC workers with PTSD and MDD, 0.51 (0.21-0.82) for those with PTSD alone, and 0.42 (−0.43 to 1.27) for workers with MDD alone. Unadjusted AQLQ scores were also significantly different across study groups (mean ± SD, 3.87 ± 1.28 for WTC workers with PTSD and MDD, 4.73 ± 1.29 for those with PTSD alone, 4.23 ± 1.64 for those with MMD alone, and 5.41 ± 1.17 for workers with no PTSD or MDD). Compared with workers without PTSD or MDD, the mean difference (95% CI) in AQLQ scores was −1.54 (−2.01 to −1.08) for WTC workers with PTSD and MDD, −0.69 (−1.04 to −0.33) for those with PTSD alone, and 1.18 (−2.18 to −0.18) for workers with MDD alone. Similarly, the rates of asthma-related ER visits or hospitalizations in the previous year were 42% for WTC workers with PTSD and MDD, 27% for workers with PTSD alone, 17% for those with MDD alone, and 9% for workers with no PTSD or MDD. The unadjusted odds ratio (95% CI) for acute asthma-related healthcare resource utilization among workers with PTSD and MDD was 7.58 (3.15-18.26), for workers with PTSD alone was 3.91 (1.81-8.43), and for those with MDD alone was 2.1 (0.23-19.09) compared with workers without PTSD or MDD.

As seen in Table 3, adjusted analyses revealed significant differences in asthma control among WTC workers with PTSD and MDD (mean adjusted difference [95% CI] in ACQ scores, 1.32 [0.85-1.80]) and with PTSD alone (mean adjusted difference [95% CI], 0.44 [0.03-0.84]), but not with MDD alone (mean adjusted difference [95% CI], 0.50 [−0.38 to 1.38]) compared with those without PTSD or MDD. Similarly, WTC workers with PTSD and MDD (mean adjusted difference [95% CI], −1.67 [−2.22 to −1.12]), PTSD alone (mean adjusted difference [95% CI], −0.56 [−2.23 to −1.12]), and MDD alone (mean adjusted difference [95% CI], −1.21 [−2.23 to −0.18]) had lower AQLQ scores compared with workers without PTSD or MDD. Adjusted odds for acute resource utilization was higher (7.61, 95% CI, 2.21-26.21) among workers with PTSD and MDD vs those without PTSD or MDD. However, no statistically significant increase in acute resource utilization was observed among WTC workers with PTSD alone (odds ratio, 2.98, 95% CI, 0.91-9.73) or MDD alone (odds ratio, 1.88, 95% CI, 0.15-24.31).

Discussion

Asthma is the single most common physical health condition and remains a major source of morbidity for WTC workers almost 20 years after exposure to the debris caused by the collapse of the WTC towers. Previous literature found a consistent association between PTSD and poor asthma control and worse quality of life.[5,6,27,28] MDD, however, although a risk factor for worse asthma outcomes in the general population, has not yet been identified as a predictor of poor asthma control in WTC responders. In this study, we found that many WTC workers with asthma have comorbid PTSD and MDD. Moreover, workers with PTSD and MDD had worse asthma morbidity than those with only one of these mental health

Table 1
Baseline Characteristics of World Trade Center Workers with Asthma According to Posttraumatic Stress Disorder and Major Depressive Disorder Status

Characteristic	PTSD and MDD	PTSD alone	MDD alone	No PTSD or MDD	*P* value
Age (y), mean ± SD	53.6 ± 7.5	53.7 ± 9.9	52.0 ± 4.6	56.2 ± 7.9	.50
Male, no. (%)	22 (71)	40 (68)	4 (67)	140 (77)	.50
Race and ethnicity, no. (%)					
Black	6 (19)	9 (16)	1 (17)	44 (24)	.01
White	3 (9.7)	21 (36)	2 (33)	71 (39)	
Hispanic	12 (38.7)	23 (40)	2 (33)	51 (28)	
Other	10 (32.3)	5 (9)	1 (17)	16 (9)	
Education, no. (%)					
Some high school	2 (7)	11 (19)	0 (0)	13 (7)	.20
High school graduate	7 (23)	5 (8)	2 (33)	39 (21)	
Some college	13 (42)	22 (38)	2 (33)	65 (35)	
College graduate	9 (29)	19 (33)	2 (33)	67 (36)	
Monthly income, no. (%)					.01
≤$3000	13 (48)	24 (48)	1 (20)	41 (24)	
>$3000	14 (52)	26 (52)	4 (80)	131 (76)	
WTC exposure, no. (%)					
Low	2 (8)	5 (13)	1 (17)	16 (12)	.30
Intermediate	15 (60)	20 (53)	4 (67)	93 (70)	
High	2 (7)	9 (24)	1 (17)	18 (13)	
Very high	6 (27)	4 (11)	0 (0)	12 (9)	
Ever smoked, no. (%)	22 (73)	48 (79)	4 (67)	132 (75)	.80
Asthma onset post 9/11, no. (%)	28 (90)	49 (85)	4 (67)	134 (82)	.40
History of intubation, no. (%)	3 (10)	1 (2)	1 (17)	0 (0)	.01
Oral steroids in the previous year, no. (%)	10 (35)	22 (37)	2 (33)	49 (27)	.40
On asthma controller medication, no. (%)	20 (59)	35 (56)	5 (83)	115 (61)	.70
Comorbidities, no. (%)					
GERD	19 (56)	40 (64)	5 (83)	125 (66)	.60
Chronic sinusitis	20 (59)	31 (49)	3 (50)	106 (56)	.80
Diabetes	7 (21)	10 (16)	2 (33)	34 (18)	.60
Hypertension	12 (35)	24 (38)	3 (50)	91 (48)	.40

Abbreviations: GERD, gastroesophageal reflux disease; MDD, major depressive disorder; no, number; PTSD, posttraumatic stress disorder; WTC, World Trade Center.

Table 2
Unadjusted Asthma Outcomes Among World Trade Center Workers With Posttraumatic Stress Disorder or Major Depressive Disorder

Characteristic	PTSD and MDD		PTSD alone		MDD alone		No PTSD or MDD
	Mean ± SD	Difference (95% CI)	Mean ± SD	Difference (95% CI)	Mean ± SD	Difference (95% CI)	Mean ± SD
ACQ Score	2.35 ± 1.12	1.16 (0.76-1.55)	1.71 ± 1.10	0.51 (0.21-0.82)	1.61 ± 1.09	0.42 (−0.43 to 1.27)	1.19 ± 1.01
AQLQ Score	3.87 ± 1.28	−1.54 (−2.01 to −1.08)	4.73 ± 1.29	−0.69 (−1.04 to −0.33)	4.23 ± 1.64	−1.18 (−2.18 to −0.18)	5.41 ± 1.17
	Percentage	OR (95% CI)	Percentage	OR (95% CI)	Percentage	OR (95% CI)	Percentage
Resource utilization	42%	7.58[a] (3.15-18.26)	27%	3.91[a] (1.81- 8.43)	17%	2.1[a] (0.23-19.09)	9%

Abbreviations: ACQ, asthma control questionnaire; AQLQ, asthma quality of life questionnaire; CI, confidence interval; MDD, major depressive disorder; OR, odds ratio; PTSD, posttraumatic stress disorder.
[a]The reference group is the group of workers without PTSD or MDD.

comorbidities.[29] These results highlight a group of WTC workers at high risk for poor asthma outcomes and suggest that mental health treatments should be an integral component of the management of asthma in these patients.

Previous studies have reported a high level of asthma exacerbation in WTC workers and exposed community members, with reports of poorly-controlled disease in more than 70% of these populations.[29] High levels of resource utilization for asthma exacerbations and major impacts on asthma-related quality of life in WTC workers with asthma have also been described, providing additional evidence of the substantial impact on well-being and the healthcare costs associated with this chronic respiratory condition.[29] PTSD has been consistently associated with increased asthma morbidity in WTC workers, firefighters, and local residents.[29,30] WTC workers with more severe PTSD symptoms are at increased risk of new-onset asthma and more severe disease[31,32]; however, even WTC-exposed individuals with subthreshold PTSD may be at increased risk of worse asthma outcomes.[28] The relationship between asthma morbidity and PTSD has also been reported among veterans and individuals in the general population with asthma.[16,33-35]

Major depressive disorder is also a common mental health condition diagnosed in many first responders, recovery workers, and community residents exposed to the WTC debris.[27] The impact of MDD on asthma morbidity is considerable. Studies in the general population of patients with asthma have found that MDD is associated with poorer quality of life, worse pulmonary function, increased health care utilization, and use of rescue medications.[36-40] However, in WTC-exposed populations, MDD has, heretofore, not exhibited a consistent link with worse asthma outcomes. In this study, we found that approximately one-third of WTC workers with asthma and PTSD had a coexisting diagnosis of MDD. Moreover, we found that the workers with comorbid PTSD and MDD had significantly worse asthma control, increased resource utilization, and poorer quality of life.

Several mechanisms may explain the observed association between mental health conditions and asthma morbidity. PTSD affects multiple organ systems as a consequence of changes in the hypothalamic-pituitary axis, the autonomic nervous system, and the immune system.[41,42] PTSD is associated with a state of basal, low-grade, systemic inflammation, which, in turn, may modulate airway inflammation, a central feature of asthma. Cognitive and behavioral mechanisms may also play a role. First, PTSD has been more strongly correlated with subjective, rather than objective, measures of asthma control. Thus, misinterpretation and overperception of symptoms may be more common among WTC workers with PTSD and may contribute to increased asthma morbidity.[43] Asthma self-management behaviors encompass several complex behaviors such as adherence to controller medications, adequate inhaler technique, use of action plans, allergen avoidance, and avoiding tobacco exposure that is critical for adequate asthma control. Studies conducted in the general population and in WTC workers with asthma have found that only 50% of patients adhere to controller therapy.[44-46] PTSD has been strongly associated with low treatment adherence in multiple chronic diseases,[47,48] thus, suggesting another potential pathway for the association between PTSD and worse asthma morbidity. MDD is also associated with systemic inflammation.[49] Moreover, research in multiple chronic diseases, including asthma, has found that patients with comorbid MDD have lower rates of adherence to treatment.[50] Thus, biobehavioral mechanisms may also explain the relationship between MDD and worse asthma control in WTC rescue workers. Taken together, the combined effects of PTSD and MDD may compound the biological and psychological impact of these conditions on asthma morbidity and control. The co-occurrence of PTSD and MDD has been consistently linked with worse outcomes in other chronic conditions. For example, a nationally representative survey reported that veterans with co-occurring PTSD and MDD were more likely to be diagnosed with cardiovascular disease, migraine, fibromyalgia, and rheumatoid arthritis than those with MDD alone and had greater odds of having a diagnosis of hypercholesterolemia and hypertension than those with PTSD alone.[51] In the same population-based study, those with comorbid PTSD-MDD were more likely to endorse current suicide ideation, lifetime suicide attempts, probable generalized anxiety and social anxiety disorders, and poor cognitive and mental health functioning and quality of life than veterans with either

Table 3
Adjusted Differences in Asthma Outcomes Among World Trade Center Workers with Posttraumatic Stress Disorder or Major Depressive Disorder

Outcome	PTSD and MDD	PTSD alone	MDD alone
	Mean difference (95% CI)	Mean difference (95% CI)	Mean difference (95% CI)
ACQ scores	1.32 (0.85-1.80)	0.44 (0.03-0.84)	0.50 (−0.38 to 1.38)
AQLQ scores	−1.67 (−2.22 to −1.12)	−0.56 (−2.23 to −1.12)	−1.21 (−2.23 to −0.18)
	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Acute resource utilization	7.61[a] (2.21-26.21)	2.98[a] (0.91-9.73)	1.88[a] (0.15-24.31)

Abbreviations: ACQ, asthma control questionnaire; AQLQ, asthma quality of life questionnaire; CI, confidence interval; MDD, major depressive disorder; OR, odds ratio; PTSD, posttraumatic stress disorder.
NOTE: Controlling for age, sex, race and ethnicity, education, income, asthma onset pre vs post 9/11, comorbidities, and WTC exposure.
[a]The reference group is the group of workers without PTSD or MDD.

PTSD or MDD alone.[52] There is a growing literature aimed at understanding factors that might help explain the experience of comorbid PTSD-MDD. Researchers have identified certain personality characteristics, namely high neuroticism (negative affectivity) and low extraversion, that may be specifically linked to co-occurring PTSD and MDD.[53] Based on shared diagnostic symptoms and biological correlates, it has also been theorized that the experience of PTSD-MDD comorbidity may actually be a phenotypic subtype of PTSD.[54] Additional information about both the inflammatory and cognitive-behavioral pathways explaining our findings would be critical to further the understanding of the phenomenology of PTSD-MDD comorbidity and to develop targeted biological therapies and cognitive-behavioral interventions to improve the outcomes of these patients.

Our study has strengths and limitations. We enrolled a well-characterized population of WTC workers with asthma and used the reference standard of the SCID to assess for PTSD and MDD. Moreover, our measures of asthma control and quality of life are well-validated tools. Acute asthma-related resource utilization was obtained by self-report; however, previous studies have reported validity in using this approach.[55,56] Our study included only WTC workers enrolled in the WTCHP, and therefore, the study results cannot be generalized to other exposed populations such as firefighters or local community members such as residents, students, business, and service members. We did not include a sample of unexposed patients with asthma; thus, we could not assess if the rates of PTSD or MDD are increased among WTC workers. However, multiple previous studies have documented the association between WTC exposure and higher rates of mental health conditions.[9,57,58] The cohort included a small number of WTC workers with MDD alone; thus, our estimates of asthma morbidity in this group could exhibit a lack of precision and should be confirmed by additional studies. Whereas we assessed for PTSD symptoms in relation to WTC exposures, we did not capture the date of onset of PTSD or MDD. Finally, the study used a cross-sectional design, which does not allow establishing causal relationships between PTSD or MDD with asthma morbidity. It may be possible that the physical and social limitation of poor asthma control can lead to or worsen symptoms of MDD or PTSD. However, previous studies of WTC-exposed workers found PTSD symptoms preceded the development of asthma.[31]

In summary, this study found that WTC workers with comorbid PTSD and MDD are at the highest risk for poor asthma outcomes. These results have direct implications for the management of WTC workers, a population experiencing a high burden of asthma. First, it highlights the importance of screening for mental health conditions, particularly for symptoms of PTSD and MDD among WTC workers with uncontrolled asthma. Relatively brief screening tools are available for these conditions, which can easily be integrated into the routine care of these patients. Second, it suggests the importance of adequately addressing mental health problems as a complementary strategy for achieving good asthma control. Further research is needed to better understand the potential biological and cognitive-behavioral pathways underlying the relationships between PTSD and MDD with increased asthma morbidity. Established treatments for MDD, specifically behavioral activation, and those for PTSD, namely, cognitive processing therapy and prolonged exposure therapy, have been successful in reducing both PTSD and MDD symptoms.[59-62] Integrated treatments focused on behavioral activation and exposure have also exhibited promise for treating comorbid PTSD and MDD.[63,64] Future studies should also evaluate the effectiveness of integrated asthma-mental health interventions for improving the outcomes of WTC workers.

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