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Research Paper

Association of PTSD history with confusion or memory loss among World Trade Center Health Registry enrollees

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ABSTRACT

Background: Burgeoning research suggests that people exposed to the 9/11/2001 terrorist attacks in New York City (NYC) may be at greater risk for cognitive impairment due to a variety of potential exposures. We investigated whether posttraumatic stress disorder (PTSD) history was associated with self-reported confusion or memory loss (CML) among World Trade Center Health Registry enrollees.

Methods: The study sample included enrollees who completed all five wave surveys (W1 in 2003–04 through W5 in 2020–21), were between the ages of 35 and 64 during W3-W5, and had no history of stroke or dementia (N = 11,432). We categorized PTSD history during W1-W3 as chronic-high, increased, decreased, or resilient-low with trajectory analysis. Generalized estimating equations modeling was used for the repeated measures analysis of the outcome, CML.

Results: Compared to those in the resilient-low PTSD group, those in the decreased and increased PTSD groups were at over 52% greater risk of reporting CML; those in the chronic-high PTSD group had between a 1.62 and 1.92 times greater risk of CML than the resilient-low PTSD group, with non-rescue/recovery workers having greater risk on average. PTSD history was also associated with elevated risk of more severe CML-related outcomes in W5 – specifically, experiencing worsening symptoms and functioning in daily life.

Limitations: CML symptoms are self-reported, and generalizability of results may be limited.

Conclusions: These findings suggest that survivors with PTSD should be monitored for cognitive issues, including CML. Effective treatment of PTSD may have benefits beyond mitigation of PTSD symptoms.

1. Introduction

Individuals who were exposed to the 9/11/2001 terrorist attacks in New York City have been shown to be at elevated risk for a variety of adverse health outcomes (Perlman et al., 2011; Gargano et al., 2018; Smith et al., 2019; Boffetta et al., 2022; Mears et al., 2022). There are numerous disaster-related exposures that may be associated with a greater risk of cognitive issues for the 9/11-impacted population. Many survivors of the attacks have experienced psychological trauma (Smith et al., 2019), been exposed to environmental contaminants (Perlman et al., 2011; Mears et al., 2022), and have chronic physical and mental health issues related to their experiences on 9/11 (Gargano et al., 2018). As the cohort of survivors continues to age, there is growing scientific interest in whether this group is more likely to have symptoms of mild cognitive impairment (Clouston et al., 2022).

Posttraumatic stress disorder (PTSD) is a mental health disorder that continues to affect this population, over twenty years later (Trivedi et al., 2022). PTSD can also be a risk factor for negative health effects, including cognitive issues (Ashbaugh et al., 2018; Waldhauser et al., 2018; Saadi et al., 2021). Burgeoning research specific to the 9/11 survivor population suggests that there may be greater risk of mild cognitive impairment or subjective cognitive issues in this group (Clouston et al., 2016, 2017, 2019; Singh et al., 2019). One cohort study of 9/11 survivors concluded that having other mental health conditions in addition to PTSD contributed to the likelihood of reporting confusion or memory loss (CML) (Alper et al., 2020).

In the present study, we sought to understand to what degree one's history with 9/11-related PTSD is predictive of future CML risk, as well as how PTSD history affects more severe outcomes or functionality related to CML. We hypothesized that survivors with chronic-high PTSD (Wave 1-Wave 3) would be more likely to report CML at future timepoints (Wave 3-Wave 5) than those with increased, decreased, or resilient-low PTSD, under the assumption that having PTSD for a longer period of time would lead to greater risk of cognitive issues. We also

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hypothesized that those with chronic-high PTSD (Wave 1-Wave 4) would be more likely to have more severe outcomes related to CML (Wave 5), such as functional impairment. The results of the present study may have clinical implications for clinicians who work with the 9/11-exposed population: expansion of knowledge about how PTSD impacts cognition, which may lead to specific decisions about screening and treatment.

2. Methods

2.1. Data and participants

The World Trade Center Health Registry (WTCHR) is a longitudinal cohort study of 9/11 survivors – rescue/recovery workers, area residents and workers, and passers-by – who were exposed to the attacks in New York City (N = 71,424). For additional information on the Registry cohort, please refer to Brackbill et al. (2006), Farfel et al. (2008). Our study sample included World Trade Center Health Registry enrollees who completed all five major wave health surveys (Wave 1 in 2003–04, Wave 2 in 2006–07, Wave 3 in 2011–12, Wave 4 in 2015–16, and Wave 5 in 2020–21); those who were between the ages of 35 and 64 during Wave 3 through Wave 5; those without a history of stroke or Alzheimer's disease or other dementia; and those without missing or invalid data for key confusion or memory loss variables (Wave 3-Wave 5) and PTSD measures (Wave 1-Wave 3). The total study sample was 11,432. This study was approved through the NYC DOHMH Institutional Review Board.

2.2. Measures

Probable PTSD was measured using the PTSD Checklist-Specific (PCL-S) scale measured during the Wave 1 through Wave 4 surveys (Wilkins et al., 2011). The PCL-S instructions were specific to respondents' experiences on 9/11 and assessed 17 self-reported symptoms of PTSD. The items relate to symptoms listed in the Diagnostic and Statistical Manual of Mental Disorders: DSM-IV, 1994. The PCL-S is a well-validated scale used for screening purposes, with good internal consistency and test-retest reliability, among other psychometric properties (Wilkins et al., 2011). PTSD history was used as a predictor variable in our first statistical model, and four groups were created using trajectory analysis, classified as follows: low-resilient (group with consistently low PCL scores during Wave 1-Wave 3), decreasing (group showing PCL scores decreasing during Wave 1-Wave 3), increasing (group showing increasing PCL scores during Wave 1-Wave 3), and chronic-high (group with consistently high PCL scores at all three waves during Wave 1-Wave 3). The PTSD history predictor variable for the second group of models was coded similarly, save for the addition of Wave 4 PTSD status. The second models included an additional wave of PTSD data because the outcomes were specific to Wave 5, and it granted additional exposure information.

Self-reported confusion or memory loss (CML) was assessed at three timepoints: Wave 3, Wave 4, and Wave 5. The outcome in the first statistical model was based on a dichotomous (yes/no) variable coded from enrollees' responses to the following question: "During the last 12 months, have you experienced confusion or memory loss, other than occasionally forgetting the name of someone you recently met?" In the second model, more in-depth questions about confusion or memory loss from Wave 5 served as outcome variables, among enrollees who reported CML in the first models. Specifically, worsening CML was categorized as a dichotomous outcome from the question: "During the last 12 months, has your confusion or memory loss happened more often or gotten worse?" Having less functioning due to CML was categorized as responding "Always," "Usually," or "Sometimes" to questions about giving up or needing assistance with day-to-day household activities or chores, or interference with the ability to work, volunteer, or engage in social activities outside the home. Whether or not the enrollee or someone else had spoken to a healthcare professional about their CML was another dichotomous outcome measured in Wave 5.

Demographic characteristics defined in our study sample were self-reported and included age group, sex, race/ethnicity, marital status, educational attainment, household income, and whether the enrollee was a rescue/recovery worker (RRW) related to 9/11. Covariates in the statistical models included the demographic characteristics as well as a dichotomized measure of social support (lower vs. higher); diagnoses of an alcohol or drug use problem, anxiety disorder, or depression (ever/never); current smoking status (yes/no); employment status (currently employed or not); current physical activity (yes/no); number of significant life stressors (0 vs. 1 vs. 2 or more); and number of post-9/11 traumatic events (0 vs. 1 vs. 2 or more). More information about the survey questions, response options, and categorizations can be found in Supplemental Table 1.

2.3. Statistical analysis

First, we described the study sample regarding the main predictor (PTSD history during Wave 1-Wave 3), main outcome (CML during

Table 1
Description of study sample, N=11,432.

Characteristic	Overall (N=11,432) N	%
Reported confusion or memory loss (CML)		
Wave 3	3827	33.5%
Wave 4	4078	35.7%
Wave 5	3308	28.9%
PTSD history (Wave 1-Wave 3)		
Chronic-high	525	4.6%
Increased	1486	13.0%
Decreased	983	8.6%
Resilient-low	8438	73.8%
Age group (Wave 5)		
43-50	2392	20.9%
51-57	4013	35.1%
58-64	5027	44.0%
Sex		
Male	7312	64.0%
Female	4120	36.0%
Race/ethnicity[†]		
Asian/Pacific Islander	493	4.3%
Black non-Hispanic	880	7.7%
Hispanic	1212	10.6%
Multiple races	175	1.5%
Other race	108	0.9%
White non-Hispanic	8564	74.9%
Marital status (Wave 5)		
Married or living with partner	8633	75.5%
Divorced or separated	1244	10.9%
Widowed	173	1.5%
Never married	1348	11.8%
Missing	*34*	*0.3%*
Educational attainment (Wave 5)		
Less than high school	141	1.2%
High school graduate	1246	10.9%
Some college	3370	29.5%
College graduate or higher	6622	57.9%
Missing	*53*	*0.5%*
Eligibility group		
Rescue/recovery worker	5937	51.9%
Non-rescue/recovery worker	5495	48.1%
Household income (Wave 5)		
<$25,000	453	4.0%
$25,000 - $49,999	756	6.6%
$50,000 - $74,999	1187	10.4%
$75,000 - $149,999	4233	37.0%
≥$150,000	4398	38.5%
Missing	*405*	*3.5%*

[†] Race/ethnicity groups included under "Other race" include unknown race/ethnicity, American Indian, and Alaska Native.

Wave 3-Wave 5), and key demographic characteristics using descriptive statistics: counts and proportions (see Table 1). Next, we used multivariable Poisson generalized estimating equations modeling to conduct a repeated measures analysis of the outcome – CML in Wave 3-Wave 5 – using PTSD history during Wave 1-Wave 3 as the predictor (resilient-low vs. decreased vs. increased vs. chronic-high). This allowed us to calculate risk ratios signifying risk of developing CML based on PTSD, controlling for the covariates of interest (see Table 2). Eligibility group (i.e., RRW vs. non-RRW status) showed a significant interaction with PTSD history, leading us to present Table 2 results stratified by these two groups. In our final models, due to convergence issues with log-binomial modeling, we used multivariable modified Poisson regression with robust error variance to assess whether PTSD history during Wave 1-Wave 4 was predictive of more severe CML outcomes among a subsample of our study population – those who reported CML at Wave 5 (see Table 3). The three main CML outcomes were worsening CML in the past year, less functioning due to CML, and having spoken to a healthcare professional about one's CML. Key covariates of interest were also controlled for in these models as potential confounders; model referent groups are specified in Tables 2 and 3. A 2-sided *p*-value of <0.05 was considered statistically significant. Analyses were completed using SAS version 9.4.

Table 2
Risk of developing CML based on PTSD history and other covariates, stratified by eligibility group.

	RRWs				Non-RRWs			
	Risk ratio	Lower CI	Upper CI	*p-value*	Risk ratio	Lower CI	Upper CI	*p-value*
Wave number								
Wave 3	Ref			*<0.0001*†	Ref			*<0.0001*†
Wave 4	1.04	1.00	1.08		1.10	1.05	1.15	
Wave 5	0.86	0.82	0.90		0.86	0.82	0.90	
PTSD history (Wave 1-Wave 3)								
Chronic-high	1.62	1.49	1.76	*<0.0001*†	1.92	1.73	2.12	*<0.0001*†
Increased	1.55	1.45	1.65		1.69	1.56	1.83	
Decreased	1.53	1.41	1.66		1.52	1.40	1.66	
Resilient-low	Ref				Ref			
Age group (Wave 5)								
54-64 years	1.02	0.97	1.08	*0.4557*	1.02	0.96	1.09	*0.4826*
43-53 years	Ref				Ref			
Social support (Wave 3)								
Higher	0.79	0.75	0.84	*<0.0001*†	0.79	0.74	0.84	*<0.0001*†
Lower	Ref				Ref			
Sex								
Male	1.05	0.98	1.12	*.1559*	1.12	1.05	1.19	*<0.001*†
Female	Ref				Ref			
Race/ethnicity††								
White non-Hispanic	Ref			*0.0877*	Ref			*0.0807*
Black non-Hispanic	0.87	0.77	0.99		0.90	0.82	0.99	
Hispanic	0.98	0.91	1.06		1.06	0.97	1.15	
Asian/Pacific Islander	1.13	0.94	1.36		1.00	0.88	1.13	
Multiple races	1.13	0.95	1.33		1.10	0.90	1.35	
Other race	1.08	0.88	1.32		1.04	0.80	1.36	
Marital status (Wave 3)								
Divorced or separated	0.89	0.83	0.95	*<0.001*†	0.95	0.88	1.03	*<0.01*†
Widowed	0.80	0.56	1.13		0.86	0.67	1.10	
Never married	0.88	0.80	0.96		0.87	0.80	0.94	
Married or living with partner	Ref				Ref			
Educational attainment (Wave 4)								
Less than high school	1.09	0.91	1.30	*0.0259*†	1.22	0.99	1.51	*<0.01*†
High school graduate	1.10	1.02	1.19		1.16	1.05	1.28	
Some college	1.08	1.02	1.15		1.14	1.06	1.23	
College graduate or higher	Ref				Ref			
Household income (Wave 4)								
<$25,000	1.15	1.02	1.30	*0.0230*†	1.10	0.97	1.24	*0.5266*
$25,000 - $49,999	1.12	1.00	1.24		1.07	0.96	1.20	
$50,000 - $74,999	1.13	1.03	1.23		1.01	0.91	1.12	
$75,000 - $149,999	1.11	1.04	1.18		1.04	0.96	1.12	
≥$150,000	Ref				Ref			
Alcohol/drug diagnosis (Wave 4)	1.12	1.03	1.22	*0.0141*†	1.13	1.01	1.26	*0.0381*†
Depression diagnosis (Wave 3)	1.21	1.13	1.29	*<0.0001*†	1.26	1.18	1.36	*<0.0001*†
Anxiety diagnosis (Wave 3)	1.16	1.09	1.24	*<0.0001*†	1.07	0.99	1.14	*0.0838*
Current smoker (Wave 3)	1.03	0.96	1.11	*0.3671*	1.01	0.93	1.10	*0.7672*
Not employed (Wave 3)	1.06	1.00	1.13	*0.0491*†	0.97	0.89	1.04	*0.3809*
Not physically active (Wave 3)	1.12	1.06	1.19	*<0.0001*†	1.07	1.00	1.14	*0.0471*†
Life stressors (Wave 3)								
0	Ref			*<0.0001*†	Ref			*<0.0001*†
1	1.13	1.05	1.21		1.24	1.14	1.35	
2 or more	1.27	1.19	1.36		1.40	1.29	1.52	
Post 9/11 traumas (Wave 3)								
0	Ref			*<0.0001*†	Ref			*<0.0001*†
1	1.11	1.04	1.19		1.12	1.04	1.21	
2 or more	1.20	1.13	1.27		1.26	1.16	1.37	

Note: Ref = referent; CML = confusion or memory loss; CI = 95% confidence interval; PSTD = posttraumatic stress disorder.
† Statistically significant difference at p<0.05 level.
†† Race/ethnicity groups included under "Other race" include unknown race/ethnicity, American Indian, and Alaska Native.

Table 3
Risk of more severe CML outcomes in Wave 5 based on PTSD history and other covariates.

	Worsening CML		Less functioning due to CML		Speaking to doctor about CML	
	Rel. risk (95% CI)	*p-value*	Rel. risk (95% CI)	*p-value*	Rel. risk (95% CI)	*p-value*
PTSD history (Wave 1-Wave 4)						
Chronic-high	1.23 (1.13, 1.34)	*<0.0001*†	1.48 (1.33, 1.64)	*<0.0001*†	1.04 (0.86, 1.26)	*0.6468*
Increased	1.18 (1.08, 1.29)		1.59 (1.43, 1.77)		1.05 (0.87, 1.27)	
Decreased	1.18 (1.05, 1.32)		1.27 (1.08, 1.51)		0.88 (0.67, 1.15)	
Resilient-low	Ref		Ref		Ref	
Age group (Wave 5)						
54-64 years	1.01 (0.94, 1.07)	*0.8622*	1.00 (0.92, 1.08)	*0.9253*	0.95 (0.84, 1.09)	*0.4803*
43-53 years	Ref		Ref		Ref	
Social support (Wave 4)						
Higher	0.95 (0.89, 1.01)	*0.1092*	0.80 (0.73, 0.88)	*<0.0001*†	1.15 (1.00, 1.31)	*0.0480*†
Lower	Ref		Ref		Ref	
Sex						
Male	0.95 (0.88, 1.02)	*0.1260*	1.06 (0.97, 1.17)	*0.1932*	0.83 (0.72, 0.96)	*0.0132*†
Female	Ref		Ref		Ref	
Race/ethnicity††						
White non-Hispanic	Ref	*0.7024*	Ref	*<0.01*†	Ref	*0.1906*
Black non-Hispanic	0.91 (0.80, 1.04)		1.27 (1.11, 1.45)		0.97 (0.75, 1.26)	
Hispanic	0.96 (0.88, 1.05)		1.20 (1.08, 1.33)		0.86 (0.71, 1.04)	
Asian/Pacific Islander	1.04 (0.89, 1.21)		1.20 (0.99, 1.46)		0.69 (0.47, 1.02)	
Multiple races	0.95 (0.76, 1.19)		1.00 (0.75, 1.34)		0.92 (0.58, 1.46)	
Other race	0.95 (0.72, 1.25)		1.02 (0.74, 1.40)		0.76 (0.40, 1.43)	
Marital status (Wave 4)						
Divorced or separated	0.96 (0.88, 1.05)	*0.7504*	0.99 (0.89, 1.10)	*0.8970*	0.89 (0.74, 1.07)	*0.5208*
Widowed	0.93 (0.70, 1.24)		0.99 (0.74, 1.33)		1.06 (0.68, 1.66)	
Never married	0.97 (0.88, 1.07)		0.95 (0.84, 1.08)		1.02 (0.84, 1.26)	
Married or living with partner	Ref		Ref		Ref	
Educational attainment (Wave 4)						
Less than high school	1.07 (0.86, 1.35)	*0.0837*	1.38 (1.13, 1.70)	*<0.0001*†	1.10 (0.70, 1.72)	*0.4712*
High school graduate	1.04 (0.94, 1.15)		1.31 (1.17, 1.48)		0.86 (0.70, 1.06)	
Some college	1.10 (1.02, 1.17)		1.15 (1.05, 1.27)		0.96 (0.84, 1.11)	
College graduate or higher	Ref		Ref		Ref	
Eligibility group						
Rescue/recovery worker	1.02 (0.95, 1.09)	*0.6094*	1.09 (1.00, 1.20)	*0.0566*	1.18 (1.02, 1.36)	*0.0230*†
Non-rescue/recovery worker	Ref		Ref		Ref	
Household income (Wave 4)						
<$25,000	0.88 (0.77, 1.01)	*0.2075*	1.46 (1.23, 1.74)	*<0.0001*†	1.36 (1.05, 1.76)	*0.0155*†
$25,000 - $49,999	0.91 (0.80, 1.03)		1.48 (1.25, 1.75)		1.32 (1.04, 1.66)	
$50,000 - $74,999	0.93 (0.83, 1.03)		1.47 (1.26, 1.72)		1.05 (0.84, 1.31)	
$75,000 - $149,999	0.91 (0.85, 0.99)		1.38 (1.21, 1.58)		0.95 (0.80, 1.13)	
≥$150,000	Ref		Ref		Ref	
Alcohol/drug diagnosis (Wave 4)	1.06 (0.95, 1.17)	*0.3171*	1.01 (0.89, 1.15)	*0.8656*	1.17 (0.97, 1.42)	*0.1320*
Depression diagnosis (Wave 4)	1.07 (1.00, 1.16)	*0.0610*	1.13 (1.02, 1.25)	*0.0224*†	1.51 (1.29, 1.77)	*<0.0001*†
Anxiety diagnosis (Wave 4)	1.03 (0.95, 1.10)	*0.4906*	1.14 (1.04, 1.25)	*<0.01*†	1.29 (1.11, 1.50)	*<0.001*†
Current smoker (Wave 4)	1.05 (0.96, 1.16)	*0.2737*	1.02 (0.92, 1.14)	*0.6752*	1.00 (0.82, 1.23)	*0.9638*
Not employed (Wave 4)	0.97 (0.90, 1.04)	*0.4105*	1.09 (1.00, 1.20)	*0.0607*	1.26 (1.10, 1.44)	*<0.01*†
Not physically active (Wave 4)	1.08 (1.01, 1.15)	*0.0213*†	1.22 (1.12, 1.32)	*<0.0001*†	1.12 (0.99, 1.28)	*0.0847*
Life stressors (Wave 4)						
0	Ref	*<0.01*†	Ref	*0.0340*†	Ref	*0.1948*
1	1.02 (0.94, 1.10)		1.00 (0.90, 1.10)		1.15 (0.99, 1.34)	
2 or more	1.14 (1.06, 1.23)		1.12 (1.02, 1.24)		1.04 (0.89, 1.22)	
Post 9/11 traumas (Wave 4)						
0	Ref	*<0.01*†	Ref	*0.01*†	Ref	*<0.001*†
1	0.98 (0.90, 1.06)		1.10 (0.99, 1.22)		1.07 (0.90, 1.27)	
2 or more	1.12 (1.04, 1.20)		1.18 (1.07, 1.30)		1.35 (1.17, 1.57)	

Note: Ref = referent; CML = confusion or memory loss; rel. risk = relative risk; CI = confidence interval; PSTD = posttraumatic stress disorder.
† Statistically significant difference at p<0.05 level.
†† Race/ethnicity groups included under "Other race" include unknown race/ethnicity, American Indian, and Alaska Nativ

3. Results

Among the 11,432 WTCHR enrollees in the study sample, those reporting CML in the past year ranged from 28.9% to 35.7% during Wave 3, Wave 4, and Wave 5 (see Table 1). Almost three-quarters of the sample (73.8%) were classified as having resilient-low PTSD history during Wave 1-Wave 3, compared to 8.6% in the "decreased PTSD history" group, 13.0% in the "increased PTSD history" group, and 4.6% in the "chronic-high PTSD" group. The sample was mostly white non-Hispanic (74.9%), male (64.0%), married or living with partner (75.5%), a college graduate (57.9%), and from a higher income household, defined as greater than or equal to $150,000 (38.5%). The sample was about evenly split regarding Registry eligibility group; 51.9% were rescue/recovery workers, while 48.1% were part of the other groups, including but not limited to lower Manhattan residents, area workers, and passers-by. All enrollees in the sample were between the ages of 43 and 64 years at Wave 5 due to the study's inclusion criteria.

The generalized estimating equations models were used to calculate the risk of developing CML based on PTSD history (see Table 2). Compared to those who were in the resilient-low PTSD group during Wave 1-Wave 3, those in the other groups were at greater risk of reporting CML during Wave 3-Wave 5. For RRWs, the risk was over 50% greater for the decreased, increased, and chronic-high PTSD groups (risk ratio (RRA): 1.53; 95% confidence interval (CI): 1.41, 1.66 for decreased

PTSD). The risk ratio was a bit higher for the increased (RRA: 1.55; 95% CI: 1.45, 1.65) and chronic-high (RRA: 1.62; 1.49, 1.76) PTSD groups, though not by a large margin. The risk ratio estimates for non-RRWs did demonstrate a possible dose-response effect, however. Those in the decreased PTSD group were at 52% increased risk for CML, and those in the increased PTSD group showed 69% greater risk; the chronic-high group was at almost twice the risk of reporting CML than the resilient-low PTSD group (RRA: 1.92; 95% CI: 1.73, 2.12). PTSD history was the strongest risk factor in each model, though social support was a strong protective factor against risk of CML (RRA: 0.79 for both RRWs and non-RRWs). Those with a college degree or higher level of educational attainment were less likely to report CML during Wave 3-Wave 5 than those with lower levels of educational attainment.

A history of certain health conditions or health behaviors were also significant predictors in both models. Having ever been diagnosed with an alcohol or drug issue or depression was associated with greater risk of having CML in our study sample (RRW RRA: 1.12 and 1.21, respectively and non-RRW RRA: 1.13, and 1.26, respectively). Having been diagnosed with anxiety was significantly associated with greater risk of CML among RRWs (RRA: 1.16; 95% CI: 1.09, 1.24), but the effect was less apparent in non-RRWs (RRA: 1.07; 95% CI: 0.99, 1.14). Those who reported being less physically active were at 7% to 12% increased risk for CML. Having a history of recent life stressors (e.g., inability to pay for food or housing, losing a job, or serious legal problems) or a traumatic experience post-9/11 (e.g., having life threatened by a disaster, violent attack, or a serious illness) was also associated with greater risk of CML, with a dose-response effect evident for 1 event/experience or 2 or more – effects seen in both the RRW and non-RRW groups.

Regarding risks for more severe CML-specific outcomes among those who reported CML at Wave 5 ($N = 3{,}308$), our modified Poisson models demonstrated that PTSD history was a significant predictor of having worsening CML over the past year, as well as less functioning due to CML (see Table 3). There were especially strong relative risk estimates for functioning (relative risk (RRI): 1.59 for the increased PTSD group and 1.48 for the chronic-high PTSD group). The relative risks for worsening CML over the past year were 1.18 for those with decreased and increased PTSD from Wave 1-Wave 4 and 1.23 for those with chronic-high PTSD (95% CI: 1.13, 1.34). PTSD history was not a significant predictor in whether someone with CML had spoken to a healthcare professional about their symptoms, however.

Other covariates beyond PTSD history were significantly associated with the risk of having more severe CML outcomes in Wave 5. Those who reported being less physically active were significantly more likely to report worsening CML during the past year (RRI: 1.08; 95% CI: 1.01, 1.15). Those who had experienced two or more life stressors or post-9/11 traumatic events were at greater risk for worsening CML symptoms (RRI: 1.14 and 1.12, respectively). In addition, other covariates were strongly related to risk of having less functioning due to CML as well: having lower educational attainment, having lower household income, history of depression or anxiety diagnosis, identifying as Black or Hispanic, having less social support, not being physically active, and having experienced two or more life stressors or post-9/11 traumatic events. Significant covariates associated with the "risk" of having spoken to a healthcare provider about one's CML symptoms included being a rescue/recovery worker and having a history of a depression or anxiety diagnosis, among others.

4. Discussion

Our results suggest that history of 9/11-related PTSD is related to one's risk of reporting confusion or memory loss. Being classified in any PTSD group other than resilient-low was associated with between 52% and 92% greater risk of experiencing CML symptoms. The effects of increased, decreased, or chronic-high PTSD history were evident in both RRWs and non-RRWs, but the effects were more pronounced among non-RRWs. Other covariates were also significant predictors of CML risk (e.g., social support, educational attainment, and history of depression, anxiety, or alcohol/drug disorder), though none had as large of an of an effect as PTSD. A higher level of social support also stood out as having a protective effect against CML, with an over 20% decrease in risk. Having experienced other specific life stressors or other traumatic events post-9/11 also elevated one's risk of CML, ranging from approximately 11% to 26%.

These findings add to the literature, supporting others' conclusions that PTSD contributes to cognitive issues (Yaffe et al., 2010; Clouston et al., 2016; Wang et al., 2016; Aloni et al., 2018; Bonanni et al., 2018; Cook and Simiola, 2018). There is also growing evidence that PSTD symptom severity is correlated with worse cognitive functioning (Ainamani et al., 2017; Clouston et al., 2019). Some PTSD symptoms are focused on the memory domain of cognition, which offers a biologically plausible explanation for how someone experiencing PTSD may have impaired memory functioning (Sumner et al., 2017; Waldhauser et al., 2018; Torres-Berrio and Nava-Mesa, 2019; Saadi et al., 2021). PTSD is also associated with sleep disturbances (e.g., nightmares), which can impact one's cognitive abilities (Mohlenhoff et al., 2017). Those with PTSD are more likely to have comorbid mental health conditions, such as depression or substance use disorders (Ashbaugh et al., 2018; Kang et al., 2019), and studies have shown that people with more conditions are at greater risk for cognitive impairment (Flatt et al., 2018; Yaffe et al., 2019; Alper et al., 2020). It is well-established that the 9/11 survivor population has a high prevalence of PTSD, but beyond exposure to traumatic events, many were also exposed to environmental contaminants – glass fibers, asbestos, lead, dioxins, particulate matter, industrial solvents, among numerous others (Lioy et al., 2002; Perlman et al., 2011; Clouston et al., 2022; Mears et al., 2022). Whether exposure to these substances (the level of exposure varying widely) is directly related to development of cognitive issues is a growing area of research. One study comparing women with PTSD to those without PTSD found higher level of inflammatory markers in the brains of those with PTSD, suggesting that inflammation may play a role in worsening cognitive function (Imai et al., 2018). In a cross-sectional study of middle-aged and older adults in Los Angeles, researchers found that greater levels of ambient air pollutants were associated with worse outcomes in certain cognitive testing domains (Gatto et al., 2014). Other studies have found similar results for risk of developing mild cognitive impairment after long-term exposure to traffic-related air pollution (Ranft et al., 2009).

Another aspect of our analysis was examining whether PTSD history during Wave 1 through Wave 4 was associated with risk of more severe CML outcomes in Wave 5, among those with CML at Wave 5. We found that all PTSD history groups aside from resilient-low were significantly associated with having less functioning (e.g., ability to perform chores). They were also associated with having worsening CML symptoms over the past year; there was greater risk of having functioning issues than worsening CML symptoms. Those with decreased, increased, or chronic-high PTSD histories were not more likely to speak about their symptoms with a doctor compared to those in the low-resilient PTSD group, though other covariates in the model were associated with increased likelihood of talking to a doctor, such as female sex, being a rescue/recovery worker, and having a history of depression or anxiety. Results from this analysis point towards the notion that effective treatment of PTSD would improve day-to-day functioning of 9/11 survivors – specific to cognitive issues, but likely in other respects as well.

This study had several strengths and limitations. The longitudinal cohort design allows us to be confident in the temporality of the exposures and outcomes of interest – though there is a possibility of a bit of overlap with PTSD status and CML symptoms measured at Wave 3. High response rates to Registry surveys allows us to analyze a large sample of data, providing stability in our statistical estimates. Our findings are also in line with a growing group of literature on cognitive issues and symptoms among the 9/11 survivor population (Clouston et al., 2017; Seil et al., 2019; Singh et al., 2019; Alper et al., 2020; Diminich et al.,

2021; Stein et al., 2021). Some limitations of this study include that the cognitive symptoms are self-reported. However, research on self-reported cognitive challenges or memory issues has shown that these measures likely capture and/or predict true outcomes (Kryscio et al., 2014; Chao, 2017) and often fall in line with findings from objective measurements, particularly for those with severe symptoms (Farias et al., 2005; Caracciolo et al., 2013; Chao, 2017). The Wave 5 survey was also in the field during the early period of the COVID-19 pandemic, but the survey was drafted prior to the existence of COVID-19. For this reason, we were unable to account for the possibility of COVID infection being related to CML symptoms in Wave 5. The probable PTSD scale (PCL-S) also relies upon self-reported symptoms, though it has strong and widely accepted psychometric properties (Blanchard et al., 1996; Wilkins et al., 2011). Based on the data available, we were unable to examine whether there is a bidirectional association between PTSD and CML, as the first time that CML was assessed was during Wave 3. Unmeasured confounding factors may affect the observed association between the exposure and outcome of interest. Another limitation to be considered is that generalizability may be limited, as this is a highly specific population. Finally, self-selection bias may be present in this study because the sample consisted of enrollees who participated in all five wave surveys – there has been attrition in the cohort over the years.

In our study sample, the prevalence of CML symptoms ranged from 28.9% to 35.7% during the Wave 3 to Wave 5 time period. Its frequent occurrence in a middle-aged sample of survivors may point towards a growing issue as the cohort continues to age. There may be high rates of cognitive issues or dementia to come among this population, especially among the rescue/recovery worker group (Clouston et al., 2019). Given the association between PTSD history and self-reported confusion or memory loss, it is possible that successful treatment of PTSD symptoms may help to prevent future CML. In fact, in some cases, people may be able to recover from their cognitive issues if certain health conditions (in this case, PTSD) are treated (Adams et al., 2013). Specifically, Kent et al. (2011) found improvements in executive functioning and memory in a group who received a resilience-focused PTSD treatment compared to a waitlist control group (Kent et al., 2011). Others have found improvements in executive functioning following PTSD treatment as well (Walter et al., 2010). This information may be important for 9/11 survivors to be aware of – particularly those with PTSD – as well as clinicians who treat 9/11 survivors. While the symptoms captured by the CML question may have similarities with those of diagnosed conditions such as mild cognitive impairment or dementia, they are not necessarily precursors to those conditions.

The results from this study suggest that timely, high quality, effective treatment of PTSD might have benefits that surpass those related to PTSD alone. Over twenty years past the events of 9/11, there is still a notable need for evidence-based identification and treatment of PTSD among this population (Lowe et al., 2023). Whether cognitive testing should be integrated into annual monitoring exams for WTC Health Program members is debatable given the additional clinician time and resources that would be required, though these results should raise awareness of the prevalence of CML among those with PTSD – even among those who are middle-aged. Treatment of PTSD is a priority, but individuals may also consider modifiable lifestyle changes that are associated with better cognitive functioning (e.g., increasing physical activity, minimizing alcohol consumption, and socializing with others) (Langa et al., 2008; Huntley et al., 2018; Seil et al., 2019). Discussions about PTSD and CML symptoms and corresponding treatment plans should be centered around the patient's needs and goals for having as high of a quality of life as possible.

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Data statement

World Trade Center Health Registry data may be made available following review of applications to the Registry from external researchers.

Author contributions

Devising of research question and analytic plan: K.S., H.A., S.Y., R.B., L.M. Completion of data analysis: K.S., H.A. Manuscript drafting: K.S. Manuscript editing and finalizing: K.S., H.A., S.Y., R.B., L.M. All authors have read and agreed to the published version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jadr.2023.100655.

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