Risk of Stroke Among Survivors of the September 11, 2001, World Trade Center Disaster

Shengchao Yu, PhD, MA, Howard E. Alper, PhD, Angela-Maithy Nguyen, MPH, and Robert M. Brackbill, PhD, MPH

Objective: The aim of this study was to investigate the association between 9/11-related posttraumatic stress disorder (PTSD), dust cloud exposure, and subsequent development of stroke among 42,527 enrollees in the World Trade Center (WTC) Health Registry. **Methods:** Using four waves of longitudinal data from the WTC Health Registry surveys, we employed Cox proportional hazards regression models to assess the associations. **Results:** Incidence of stroke was higher among those with PTSD or intense dust cloud exposure than those without, and it was even higher for those who had experienced both. In fully adjusted models, participants with PTSD had an increased risk of developing stroke [adjusted hazards ratio (AHR) 1.69, 95% confidence interval (95% CI) 1.42 to 2.02], as did those with intense dust exposure (AHR 1.29, 95% CI 1.09 to 1.53). **Conclusion:** We found that individuals with 9/11-related PTSD and/or intense dust exposure may have an increased risk of developing stroke.

Keywords: 9/11 dust, cohort, disaster, posttraumatic stress disorder, stroke, survival analysis, World Trade Center

The World Trade Center (WTC) terrorist attacks on September 11, 2001 (9/11) exposed many survivors to a wide range of horrific events and resulted in severe psychological distress that lasted for years for some.[1] In addition, dust and debris resulting from the collapse of the WTC towers generated high concentrations of particulate matter that remained elevated for weeks in the WTC surrounding areas.[2–4] Both psychological stress and exposure to dust and debris caused by the airplane crash and building collapse have been shown to be associated with an increased risk of developing physical conditions such as respiratory symptoms, asthma, heart diseases, gastroesophageal reflux symptoms, and cancer.[5–8] However, whether 9/11-related posttraumatic stress disorder (PTSD) and intense dust cloud exposure are related to risk of developing stroke among WTC disaster survivors has not yet been examined.

Stroke is the fifth leading cause of death in the United States; it is also the leading cause of long-term disability and the leading preventable cause of disability.[9] Assessing the stroke burden among 9/11 survivors is an important effort given the size of the population affected by 9/11. Traumatic stress has been shown to lead to an elevated risk of cardiovascular and cerebrovascular diseases.[10–12]

Individuals with PTSD have an increased risk for hypertension, diabetes, and dyslipidemia, all of which are risk factors for stroke.[12,13] However, the epidemiological evidence on the direct association of stress or PTSD and the subsequent development of stroke are limited and inconsistent. The existing studies in this area are mainly cross-sectional and have largely focused on specific populations, such as war veterans. In addition, these studies lacked validated measures in both the exposure and outcome.[14,15] One of the few studies that examined the temporal association between PTSD and the risk of developing stroke using longitudinal data found that individuals with PTSD had an increased risk of developing stroke.[15] Among 9/11 survivors, diabetes and smoking, both risk factors of stroke, were each found to be associated with PTSD.[16,17] Several 9/11 studies also suggested an association between PTSD and increased risk of heart disease[6,18,19]; one study using New York State hospitalization data found that PTSD increased cerebrovascular disease hospitalization among male survivors of the 9/11 disaster.[20] Nevertheless, no studies have examined the risk of stroke as a function of persistence of PTSD reported many years after 9/11.

In addition to the relationship between PTSD and circulatory diseases, evidence was also found that intense exposure to 9/11 dust cloud was a risk factor for heart disease.[6,18,19] However, only one study suggested that newly diagnosed stroke tended to be more prevalent among survivors exposed to the dust and debris cloud.[21] Among general populations, it has been shown that cardiovascular morbidity and mortality are associated with particulate matter (PM) air pollution, that is, exposure to PM less than 2.5 μm in diameter (PM$_{2.5}$) over a few hours to a much longer period both may trigger cardiovascular disease related events or increase the risk for cardiovascular mortality.[22] Other studies specifically reported small but significant associations between stroke and short-term PM or gaseous exposure.[23] One of these studies indicated that the association with fine PM exposure was statistically significant only for ischemic stroke, but not for hemorrhagic stroke.[24] The crash of two aircrafts on 9/11 and the subsequent collapse of large buildings resulted in an unmeasurable amount of toxic and irritant debris, gases, and particles in Lower Manhattan, so some association between dust cloud exposure and subsequent development of stroke among 9/11 survivors is expected but has not yet been examined.

In this study, we focus on the risk of stroke among 9/11 survivors who experienced probable PTSD and had 9/11 dust cloud exposure. We hypothesized that among 9/11 survivors, there was an elevated stroke risk for those who had PTSD or who had intense dust cloud exposure, and the risk could be higher for those who experienced both. This analysis used WTC Health Registry survey data collected during 2003 to 2016.

METHODS

Study Population

The WTC Health Registry was established in 2002 to monitor the long-term health impacts of the September 11, 2001 terrorist attack on the WTC in New York City. In 2003 to 2004, the Registry conducted a health survey (Wave 1) with 71,431 enrollees. Three follow-up surveys (Waves 2 to 4) were then conducted among eligible Wave 1 enrollees in 2006 to 2007, 2011 to 2012, and

2015 to 2016. A more detailed description of the WTC Health Registry cohort and recruitment methods have been provided elsewhere.[25,26] The US Centers for Disease Control and Prevention and the New York City Department of Health and Mental Hygiene institutional review boards approved the Registry protocol, including use of the data.

Inclusion and Exclusion Criteria

This study was limited to Registry enrollees who completed at least Waves 1 and 2 because the dust cloud exposure information in this study was collected in those waves. Enrollees who were younger than 18 years on 9/11 were excluded because of the rarity of stroke at young age, and also because stroke risk, symptoms, and treatment are different between children and adults. Enrollees who reported stroke before study enrollment were also excluded. The final analytical sample for this study included 42,527 enrollees.

Study Outcome

The outcome of interest, stroke, was defined as an affirmative answer to the self-report question "Have you ever been told by a doctor or other health professional that you had stroke?" at Waves 2, 3, or 4. Those who said yes were also asked to provide year of first diagnosis of stroke. If an enrollee reported stroke at a single wave, the associated year of diagnosis was accepted as year of stroke. If an enrollee reported stroke at more than one wave, the year of diagnosis reported from the earliest wave was accepted as the year of stroke.

PTSD and Dust Cloud Exposure

Probable PTSD and 9/11 dust cloud exposure were the two key measures considered in this study. PTSD related to 9/11 was assessed using the PTSD Checklist-Specific (PCL-S), a 17-item self-reported symptom scale, which referred specifically to the events of September 11. The 17 items correspond to the Diagnostic and Statistical Manual of Mental Disorders PTSD symptoms (DSM-IV 1994). In this scale, enrollees rated the degree to which they were bothered by symptoms in the past 30 days from 1 (no symptoms) to 5 (severe). Responses to the 17 items were summed, giving a possible total score of 17 to 85. Probable PTSD (referred to as PTSD hereafter) was defined as a PCL score of at least 44 and was assessed at all four waves of Registry surveys.[27]

Dust cloud exposure on 9/11 was based on questions from the Waves 1 and 2 surveys and was classified as intense exposure versus minimal or no exposure. Intense exposure was defined as having been in the dust cloud on 9/11 and reporting at least one of five experiences: being unable to see more than a few feet; having difficulty walking or finding one's way; trouble finding shelter; being covered with dust; or not being able to hear. The "minimal or none" category consisted of those who had reported being in the dust/debris cloud but did not experience intense exposure or reported no dust cloud exposure at all.

Covariates

Sociodemographic characteristics of the study sample, such as age (on 9/11/2001), sex, race/ethnicity, education, marital status, and Registry eligibility group were included in the analytical models. Marital status was defined as partnered (married, living together) or nonpartnered (never married, widowed, divorced, or separated). Enrollees were categorized into mutually exclusive, hierarchical eligibility groups based on likelihood of exposure, with rescue/recovery workers followed by lower Manhattan residents, lower Manhattan area workers, and others including passersby and school students/staff on 9/11. Risk factors for stroke included in the present study were smoking status, history of hypertension, and history of diabetes. Smoking status was classified as "never," "former," or "current" smoker. History of hypertension and diabetes were defined as a positive answer to the self-report question

"Have you ever been told by a doctor or other health professional that you had hypertension/diabetes?" at Waves 2, 3, or 4.

Statistical Analysis

As enrollees who completed Waves 1 and 2 did not necessarily complete Waves 3 or 4, we defined four "wave completion" subgroups based on which surveys enrollees completed: a) Waves 1 to 4, b) Waves 1 to 3, c) Waves 1 and 2, d) Waves 1, 2, and 4. This categorization of the study sample was necessary to correctly characterize the study outcome, risk factors, and covariates. Cox proportional hazards regression methods were employed to investigate the association between time from enrollment in the Registry to occurrence of stroke (or censoring) and two 9/11-related risk factors: PTSD and intense dust cloud exposure, while controlling for smoking status, hypertension, diabetes, and potential confounders, including age at 9/11, sex, race/ethnicity, education, marital status, and eligibility group. In the present analysis, for enrollees in each wave completion subgroup, we selected the value of PTSD, marital status, and smoking status from the wave closest to, but preceding, the stroke occurrence because of our focus on the temporal relationship between these variables and the subsequent development of stroke. For enrollees who did not report stroke, the value of PTSD, marital status, and smoking status reported at the latest wave completed were used. As the time of stroke was reported as year only, the exact date of stroke was assigned to be June 30th of the reported year of stroke (For a few cases where the year of stroke was equal to the year of entry into the Registry, the date of stroke was assigned to be December 31st of that year so that those who entered the Registry in the second half of the year were included.) For enrollees who experienced stroke, the survival time from Registry enrollment (ie, the interview date for Wave 1) to the date of first diagnosed stroke was treated as uncensored. For enrollees who did not experience stroke, the survival time from Registry enrollment to the survey completion date of the latest wave participated was treated as censored.

The proportional hazards assumption was tested for PTSD and dust cloud exposure in separate Cox regressions from the main analyses, by creating interaction terms between each of these variables and log (time to event for stroke/censoring), and testing the statistical significance of these interactions. Statistical tests were considered significant if the associated P value was less than 0.05. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Table 1 describes the sociodemographic characteristics, physical and mental health, 9/11 dust cloud exposure of the 42,527 study participants who completed at least Waves 1 and 2 surveys (23.3% of these enrollees participated in three out of the four waves, and 60.0% participated in all four waves). The majority of the participants were aged 25 to 44 years at 9/11, male, white, and highly educated. Close to half of the participants (47.3%) performed rescue or recovery work on 9/11 and thereafter, and less than one-third of the study sample (29.7%) were exposed to 9/11 intense dust cloud. At the time preceding stroke occurrence or when the last survey was completed, participants were primarily partnered and never smokers. A relatively high percentage of participants (41.6%) reported having hypertension at some point, as compared with fewer reports of ever having diabetes (12.1%) or 9/11-related PTSD (16.3%).

The overall incidence of stroke in our sample was 1.94 per 1000 person-years, which, not surprisingly, increased with increasing age (Table 2). Stroke incidence was also estimated by two major 9/11 risk factors of interest: PTSD and intense dust cloud. Table 2 summarizes that participants with PTSD exhibited an increased incidence of stroke as compared to those without (3.53 vs 1.64 per

1000 person-years, $P < 0.001$); participants with intense dust cloud exposure displayed an increased incidence of stroke as well (2.33 vs 1.77 per 1000 person-years, $P < 0.001$). For those who reported both PTSD and intense dust cloud exposure, incidence of stroke was even higher than those who reported neither (4.30 vs 1.61 per 1000 person-years, $P < 0.001$). Stratified by age group, incidence of stroke showed the same pattern for the younger (aged 18 to 44 years) and middle-age (aged 45 to 64 years) groups, but less significantly so for the older age group (aged 65+ years), especially for intense dust cloud exposure. In age-stratified models that controlled for sociodemographic characteristics and risk factors of stroke, the results on stroke hazard were consistent with the incidence rate comparison, that is, the separate Cox regression models for age groups 18 to 44 and 45 to 64 years both showed that PTSD significantly increased the hazard of developing stroke, while PTSD was not significantly associated with risk of stroke in the model for age group 65+ (results not shown); similarly, intense dust cloud exposure only increased stroke hazard among the youngest age group (under 45 years old) in the age-stratified Cox regression models (results not shown). In summary, incidence of stroke increased with increasing age regardless of 9/11 exposure; groups who reported PTSD had significantly higher incidence rate for those under age 65; groups who reported intense dust cloud exposure had significantly higher incidence only for those under age 45, but not for the older groups.

The bottom section of Table 2 summarizes how the well-established risk factors for stroke, that is, smoking status, history of hypertension or diabetes, may interact with 9/11-related PTSD and intense dust cloud and impact stroke incidence rate. The overall stroke incidence rate increased, not surprisingly, for current and former smokers and those with hypertension or diabetes as compared with nonsmokers and those without hypertension or diabetes (eg, incidence rate increased from 0.78 for those without hypertension to 3.41 for those with hypertension). Having 9/11-related PTSD increased the stroke incidence rates for both the risk groups (smokers, those with hypertension or diabetes) and the nonrisk groups. Noticeably, having PTSD alone (without having other risk factors) could increase stroke incidence rate, and the magnitude of this increase could be larger than that for the risk groups (eg, for those without hypertension, having PTSD increased the stroke incidence rate by 2.4 times from 0.67 to 1.60, while for those with hypertension the incidence rate increased 1.7 times from 2.99 to 5.06). In comparison, the impact of intense dust cloud exposure was not as consistent or significant for different risk factor groups, and the magnitude of the increase on stroke incidence rate by having intense dust cloud exposure was overall small across all risk factor groups (less than 1.3 times).

Using Cox regression models, we further examined relationships between 9/11-related PTSD, dust cloud exposure, and risk of stroke. Excluding dust cloud exposure, Table 3 Model 1 shows that PTSD was significantly associated with the risk of developing stroke, while controlling for other risk factors and potential confounding variables [adjusted hazards ratio or AHR 1.69, 95% confidence interval (95% CI) 1.42 to 2.02]. Risk of developing stroke was also associated with older age, being a current smoker, and history of diabetes or hypertension. Model 2 considers the association between dust cloud exposure and risk of stroke, without PTSD in the model. After controlling for other factors, 9/11 dust cloud exposure still significantly increased the risk of subsequent stroke (AHR 1.30, 95% CI 1.10 to 1.53). In the final model, we included both PTSD and 9/11 dust cloud exposure to evaluate whether they were independently associated with subsequent occurrence of stroke. Results from Model 3 in Table 3 summarize very modest changes on the AHRs for PTSD and 9/11 dust cloud exposure, as compared to Models 1 and 2 wherein each factor was examined independently. Specifically in the full model, the

TABLE 1. Characteristics of the Study Population

Characteristics	Total ($N = 42,527$)	%
Age groups at 9/11		
18–24	2347	5.52
25–44	23,222	54.61
45–64	15,714	36.95
65+	1244	2.93
Sex		
Male	26,048	61.25
Female	16,479	38.75
Race/ethnicity		
Non-Hispanic white	29,939	70.40
Non-Hispanic black	4304	10.12
Hispanic	4723	11.11
Asian	2158	5.07
Multiracial/Other	1403	3.30
Education		
High school or below	8958	21.20
College graduate	24,385	57.71
Postgraduate	8911	21.09
Marital status		
Partnered	29,084	69.09
Nonpartnered	13,012	30.91
Eligibility group		
Rescue/recovery workers	19,983	47.32
Residents	5880	13.92
Area workers	14,676	34.75
Passers-by and others	1694	4.01
Smoking status		
Never	22,624	55.05
Former	13,787	33.55
Current	4683	11.40
History of hypertension		
Yes	17,637	41.59
No	24,767	58.41
History of diabetes		
Yes	5136	12.14
No	37,176	87.86
PTSD		
Yes	6858	16.29
No	35,229	83.71
9/11 dust cloud exposure		
None/minimal	29,880	70.26
Intense	12,646	29.74

World Trade Center Health Registry enrollees aged ≥18 on September 11, 2001, and participants of at least Waves 1 and 2 surveys ($n = 42,527$), New York, 2003–2016.
PTSD, posttraumatic stress disorder.

AHR for PTSD slightly decreased from 1.69 to 1.64 (95% CI 1.37 to 1.96); the AHR for dust cloud exposure slightly decreased from 1.30 to 1.20 (95% CI 1.02 to 1.42). The risk of stroke in both associations remained significant while controlling for other aforementioned factors. This final model clearly demonstrated that PTSD and 9/11 dust cloud exposure each independently increased the risk of stroke among 9/11 survivors. There was no evidence that the data violated the proportional hazards assumption.

DISCUSSION

Physical and psychological exposure to the 9/11 disaster have been shown to be associated with cardiovascular diseases in several studies.[20,28–30] Our study adds to the growing evidence of 9/11-related circulatory diseases with the findings of independently increased risk of stroke by 9/11 intense dust cloud exposure and persistent PTSD. In addition, the risk of developing stroke was even higher among those who reported both PTSD and intense dust cloud exposure.

TABLE 2. Incidence of Stroke for Different Age Groups and Risk Factors, by PTSD and Intense Dust Cloud Exposure

									By PTSD and	
									Intense Dust Exposure	
	All	**By PTSD**			**By Intense Dust Exposure**					
		Yes	**No**		**Yes**	**No**		**Both**	**Neither**	
	(N = 753)	(N = 211)	(N = 532)	P	(N = 271)	(N = 482)	P	(N = 116)	(N = 380)	P
Stroke incidence rate (IR)*	1.94	3.53	1.64	<0.001	2.33	1.77	<0.001	4.30	1.61	<0.001
IR by age										
18−44	1.06	3.06	0.74	<0.001	1.61	0.82	0.005	4.05	0.64	<0.001
45−64	2.02	3.56	1.71	<0.001	2.50	1.82	0.001	4.36	1.65	<0.001
65+	2.52	3.88	2.28	0.007	2.54	2.51	0.986	4.33	2.35	0.027
IR by smoking status										
Never	1.68	3.25	1.41	<0.001	1.90	1.59	0.15	3.33	1.38	<0.001
Former	2.01	3.48	1.73	<0.001	2.45	1.82	0.03	4.85	1.73	<0.001
Current	3.63	4.82	3.18	0.016	4.34	3.25	0.09	6.33	3.21	0.008
IR by hypertension										
No	0.78	1.60	0.67	<0.001	0.94	0.72	0.123	1.73	0.63	<0.001
Yes	3.41	5.06	2.99	<0.001	3.86	3.20	0.028	6.27	3.02	<0.001
IR by diabetes										
No	1.33	2.26	1.18	<0.001	1.61	1.21	0.004	2.90	1.14	<0.001
Yes	5.19	7.55	4.39	<0.001	5.35	5.07	0.707	8.03	4.56	0.001

World Trade Center Health Registry enrollees aged ≥18 years on September 11, 2001, and participants of at least Waves 1 and 2 surveys (n = 42,527), New York, 2003−2016.
IR, incidence rate.
*Stroke IR: stroke incidence rate per 1000 person-years.

This study has unique contributions to the study of the association of PTSD and circulatory disease in three specific areas. First, our results show that the PTSD-stroke association was significant across age groups; however, the association tends to be weaker for the older age group. Incidence rates of stroke were significantly higher (two to four times) among those with PTSD than those without PTSD in age groups 18 to 44 and 45 to 64 (3.06 vs 0.74; 3.56 vs 1.71 in Table 2), but was less different for those who were 65 years and older (3.88 vs 2.88). Results from the age-stratified Cox regression models confirmed that PTSD significantly increased hazard of developing stroke for age groups 18 to 44 and 45 to 64, but not for age group 65+. Our results indicate that factors related to

TABLE 3. Evaluation of PTSD and 9/11-Related Dust Cloud Exposure as Independent Risk Factors for Self-Reported Physician-Diagnosed Stroke

| | | | Model 1: Without Dust Exposure* | | Model 2: Without PTSD* | | Model 3: Full Model* | |
	N With Stroke	Person-Time, Years	AHR	95% CI	AHR	95% CI	AHR	95% CI
Age groups at 9/11								
18−24	6	20,011	0.35	(0.14−0.85)	0.34	(0.14−0.83)	0.35	(0.14−0.84)
25−44	224	209,278	Ref	Ref	Ref			
45−64	436	148,691	2.11	(1.77−2.52)	2.07	(1.73−2.47)	2.12	(1.77−2.52)
65+	87	9,747	6.65	(5.01−8.83)	6.45	(4.89−8.52)	6.74	(5.07−8.94)
Smoking status								
Never	344	204,947		Ref		Ref		Ref
Former	261	129,944	0.96	(0.81−1.14)	0.96	(0.81−1.14)	0.96	(0.81−1.15)
Current	137	37,743	2.04	(1.65−2.54)	2.15	(1.73−2.66)	2.03	(1.64−2.52)
History of hypertension								
Yes	570	167,235	2.48	(2.06−2.98)	2.55	(2.12−3.07)	2.46	(2.05−2.97)
No	172	219,499		Ref		Ref		Ref
History of diabetes								
Yes	253	48,789	2.22	(1.88−2.63)	2.31	(1.96−2.73)	2.22	(1.88−2.62)
No	449	337,150	Ref		Ref		Ref	
PTSD								
Yes	211	59,831	1.69	(1.42−2.02)			1.64	(1.37−1.96)
No	532	323,899	Ref					Ref
9/11 dust cloud exposure								
None/minimal	482	271,552	Ref					Ref
Intense	271	116,174			1.30	(1.10−1.53)	1.20	(1.02−1.42)

World Trade Center Health Registry enrollees aged ≥18 on September 11, 2001, and participants of at least Waves 1 and 2 surveys (n = 42,527), New York, 2003−2016.
AHR, adjusted hazards ratio; CI, confidence interval; PTSD, posttraumatic stress disorder.
*In addition to variables shown in this table, all models adjusted for other factors, including sex, race/ethnicity, education, marital status, and enrollees' eligibility group.

older age may have a larger impact on the risk of developing stroke than 9/11-related PTSD among the older age group (65+), while the significant association observed for the young and middle age groups is also consistent with the fact that the majority of our study sample were under the age of 65 at 9/11. Earlier studies of 9/11-related PTSD and heart disease did not find the association was different by age group; therefore, our study's findings suggest that examining general heart diseases and stroke separately may help better define the relative effect of PTSD and age (or age-related risk factors) on different types of circulatory disease in future analyses.

Second, this analysis demonstrates that 9/11-related PTSD not only increased the risk of developing stroke for those with other risk factors (eg, current or former smokers, people with hypertension or diabetes) but also for those without. Furthermore, the magnitude of the increased risk is even larger among individuals without other risk factors. Although it may not be surprising to observe the added risk of stroke by PTSD among certain groups, our study not only confirms the direct association of PTSD and the subsequent development of stroke but also discovers that 9/11-related PTSD alone, in the absence of other risk factors, can be an important risk for developing stroke among disaster-exposed populations.

The third area in which this paper contributes to the study of PTSD-circulatory diseases association is that longitudinal data were used in our analyses. Studies on the role of PTSD in stroke development were limited and reported inconsistent results due to small sample size, lack of longitudinal data, or inaccuracy on key measures.[14,15] The WTC Health Registry surveys provided us an opportunity to assess not only the association but also the temporal relationship between PTSD and stroke, as the study sample contained more than 42,000 enrollees with longitudinal data covering up to 14 years since 9/11. As the course of PTSD evolves over time,[31] the association between PTSD at enrollment and subsequent stroke could be different from the association between PTSD at later time points (eg, closest wave to but preceding stroke or same wave as stroke) and stroke, due to possible changes in symptomology and other contextual circumstances. As our interest centered on the association between PTSD many years after 9/11 and stroke, we chose to focus on the association between PTSD from the wave closest to, but preceding the first stroke occurrence. Indeed, we found that the hazard ratio was larger when we used the PTSD value that was close to but before stroke rather than PTSD at enrollment (results not shown). Finally, unlike most previous studies focusing on specific populations,[14,15] our findings on this relationship add to the more limited body of work among civilian populations, as the WTC Health Registry cohort is a heterogeneous group of survivors.

The other association of interest in this analysis was between intense dust cloud exposure and the risk of developing stroke. Previous research found that stroke was associated with being exposed to fine PM exposure.[23,24] Although one study suggested a potential relationship between dust cloud exposure and stroke among 9/11 survivors,[21] it is unclear whether this association is strong and significant because that study only used data from Registry Wave 1 survey and the analytical model did not control for some key covariates due to a limited number of stroke cases. Thus far, this study is the first attempt to directly assess this association by using analytical models appropriate for longitudinal data. Our results show that people with 9/11-related intense dust cloud exposure had a higher hazard of developing stroke than those with minimal or without dust exposure, but the association was only significant among the younger age group (under 45 years old) in the age-stratified models that control for sociodemographic characteristics and risk factors of stroke (results for age-stratified regression models not shown). Lack of statistical significance among the middle and older age groups might result from the fact that 9/11-related dust cloud cannot simply be categorized as PM pollution,

which is more clearly shown to contribute to cardiovascular disease. The health impact of 9/11 dust cloud is more complicated and less conclusive because it is a mixture of large and fine particles, gases, and smoke plumes released by uncontrolled combustion.[3,4] Another reason for this lack of association among those 45 years and older may be that our data did not allow us to distinguish between ischemic and hemorrhagic stroke, as some research has indicated that ischemic strokes are more likely to be associated with fine PM exposure.[24]

The results of this study should be interpreted with caution for two reasons. First, stroke was self-reported. As stroke is likely to be linked to sensory and memory problems, potential bias may be introduced by using self-reported data.[32] One previous study that examined the validity of self-reported stroke used data from a population health survey and from clinical re-examination in Norway concluded that questionnaires can be used to assess a history of stroke in epidemiological research.[32] Findings from the Health and Retirement Study suggested that misreporting of self-reported stroke was nonsystematic and provided valuable data for stroke surveillance.[33] Although these previous studies offered some level of confidence in the validity of self-reported stroke, we believe that more objectively defined end-points, such as medically confirmed cases of stroke from hospital records, are required to substantiate our findings in this particular population. This approach was conducted in a previous study that found PTSD was associated with increased cerebrovascular disease hospitalization among male survivors.[20] Our next step is to expand the scope of the study by including hospitalization data from more recent years, and to differentiate stroke by ischemic stroke and hemorrhagic stroke in analyses.

The second reason for interpreting results with caution is loss to follow-up (including those who dropped out of the study completely, those who dropped out for some but not all surveys, and those who died from stroke) between the Wave 1 and Wave 4 surveys. Given that stroke is one of the leading causes of disability in the United States, it is reasonable to assume that we may have underestimated the number of stroke cases because some of the nonparticipants might not have participated in the follow-up surveys due to stroke-related disabilities or deaths. Future studies on mortality of stroke can examine and may provide more evidence on the association. However, we do not expect our findings on the associations between PTSD, dust cloud exposure, and stroke would significantly change due to loss to follow-up based on the conclusion of a previous nonresponse bias study among the same cohort.[34]

CONCLUSION

This study prospectively investigated the role of 9/11-related PTSD and intense dust exposure in increasing the risk of stroke among a large group of 9/11 survivors. We found that PTSD and intense dust cloud exposure were each independently associated with an elevated risk of stroke; the burden of stroke was the highest among those who reported both PTSD and intense dust cloud exposure; and disaster-related PTSD alone can increase stroke risk even in the absence of other well-established risk factors. Our finding suggests inclusion of periodic assessment of PTSD and intensity of dust cloud exposure measurements in screening for stroke risk factors among 9/11 survivors, in addition to the classic risk factors of stroke.

REFERENCES

1. Perlman SE, Friedman S, Galea S, et al. Short-term and medium-term health effects of 9/11. *Lancet*. 2011;378:925–934.
2. Thurston G, Maciejczyk P, Lall R, Hwang JS, Chen LC. Identification and characterization of World Trade Center disaster fine particulate matter air pollution at a site in lower Manhattan following September 11.: ISEE-432. *Epidemiology*. 2003;14:S87–S88.

3. Landrigan PJ, Lioy PJ, Thurson G, et al. Health and environmental consequences of the World Trade Center Disaster. *Environ Health Perspect*. 2004;112:731–739.

4. Lioy PJ, Pellizzari E, Prezant D. The World Trade Center aftermath and its effects on health: understanding and learning through human-exposure science. *Environ Sci Technol*. 2006;40:6876–6885.

5. Brackbill RM, Cone JE, Farfel MR, Stellman SD. Chronic physical health consequences of being injured during the terrorist attacks on World Trade Center on September 11, 2001. *Am J Epidemiol*. 2014;179:1076–1085.

6. Jordan HT, Miller-Archie SA, Cone JE, Morabia A, Stellman SD. Heart disease among adults exposed to the September 11, 2001 World Trade Center Disaster: results from the World Trade Center Health Registry. *Prev Med*. 2011;53:370–376.

7. Li J, Brackbill RM, Stellman SD, Farfel MR, Miller-Archie SA. Gastroesophageal reflux symptoms and comorbid asthma and posttraumatic stress disorder following the 9/11 terrorist attacks on World Trade Center in New York City. *Am J Gastroenterol*. 2011;106:1933–1941.

8. Solan S, Wallenstein S, Shapiro M, et al. Cancer incidence in World Trade Center rescue and recovery workers, 2001–2008. *Environ Health Perspect*. 2013;121:699–704.

9. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics: 2017 update: a report from the American Heart Association. *Circulation*. 2017;135:E146–E603.

10. Stalnikowicz R, Tsafrir A. Stress and cardiovascular events. *Am J Emerg Med*. 2002;20:488–491.

11. Arora R. Cardiovascular manifestations of posttraumatic stress disorder. *J Natl Med Assoc*. 2007;99:642–649.

12. Spitzer C, Barnow S, Volzke H, et al. Trauma, posttraumatic stress disorder, and physical illness: findings from the general population. *Psychosom Med*. 2009;71:1012–1017.

13. Boscarino JA. A prospective study of PTSD and early-age heart disease mortality among Vietnam Veterans: implications for surveillance and prevention. *Psychosom Med*. 2008;70:668–676.

14. Coughlin SS. Post-traumatic stress disorder and cardiovascular disease. *Open Cardiovasc Med J*. 2011;5:164–170.

15. Chen MH, Pan TL, Li CT, et al. Risk of stroke among patients with posttraumatic stress disorder: nationwide longitudinal study. *Br J Psychiatry*. 2015;206:302–307.

16. Miller-Archie SA, Jordan HT, Ruff RR, et al. Posttraumatic stress disorder and new-onset diabetes among adult survivors of the World Trade Center disaster. *Prev Med*. 2014;66:34–38.

17. Welch AE, Jasek JP, Caramanica K, Chiles MC, Johns M. Cigarette smoking and 9/11-related posttraumatic stress disorder among World Trade Center Health registry enrollees, 2003-12. *Prev Med*. 2015;73:94–99.

18. Lin S, Gomez MI, Gensburg L, Liu W, Hwang SA. Respiratory and cardiovascular hospitalizations after the World Trade Center Disaster. *Arch Environ Occup Health*. 2010;65:12–20.

19. Lippmann M, Cohen MD, Chen LC. Health effects of World Trade Center (WTC) dust: an unprecedented disaster's inadequate risk management. *Crit Rev Toxicol*. 2015;45:492–530.

20. Jordan HT, Stellman SD, Morabia A, et al. Cardiovascular disease hospitalizations in relation to exposure to the September 11 2001 World Trade Center Disaster and Posttraumatic Stress Disorder. *J Am Heart Assoc*. 2013; 2:E000431.

21. Brackbill RM, Thorpe LE, DiGrande L, et al. Surveillance for World Trade Center Disaster health effects among survivors of collapsed and damaged buildings. *Morb Mortal Wkly Rep*. 2006;55:1–18.

22. Brook RD, Rajagopalan S, Pope CA, et al. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331–2378.

23. Shah ASV, Lee KK, Mcallister DA, et al. Short term exposure to air pollution and stroke: systematic review and meta-analysis. *BMJ*. 2015;350:H1295.

24. Qiu H, Sun S, Tsang H, et al. Fine particulate matter exposure and incidence of stroke: a cohort study in Hong Kong. *Neurology*. 2017; 88:1709–1717.

25. Farfel M, DiGrande L, Brackbill RM, et al. An overview of 9/11 experiences and respiratory and mental health conditions among World Trade Center health registry enrollees. *J Urban Health*. 2008;85:880–909.

26. Brackbill RM, Hadler JL, DiGrande L, et al. Asthma and posttraumatic stress symptoms 5 to 6 years following exposure to the World Trade Center terrorist attack. *JAMA*. 2009;302:502–516.

27. Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the PTSD checklist (PCL). *Behav Res Ther*. 1996;34:669–673.

28. Allegra J, Mostashari F, Rothman J, Milano P, Cochrane D. Cardiac events in New Jersey after the September 11, 2001 terrorist attack. *J Urban Health*. 2005;82:358–363.

29. Croft LB, McLaughlin M, Bander J, et al. First documentation of cardiac dysfunction following exposure to the World Trade Center disaster. *J Am Coll Cardiol*. 2010;55:A86-E810.

30. Holman EA, Silver RC, Poulin M, Andersen J, Gil-Rivas V, Mcintosh DN. Terrorism, acute stress, and cardiovascular health: a 3-year national study following the September 11th attacks. *Arch Gen Psychiatry*. 2008;65:73–80.

31. Maslow CB, Caramanica K, Welch AE, Stellman SD, Brackbill RM, Farfel MR. Trajectories of scores on a screening instrument for PTSD among World Trade Center rescue, recovery, and clean-up workers. *J Traumatic Stress*. 2015;28:198–205.

32. Engstad T, Bonaa KH, Viitanen M. Validity of self-reported stroke: the Tromso study. *Stroke*. 2000;31:1602–1607.

33. Glymour MM, Avendano M. Can self-reported strokes be used to study stroke incidence and risk factors? Evidence from the Health and Retirement study. *Stroke*. 2009;40:873–879.

34. Yu S, Brackbill RM, Stellman SD, Ghuman S, Farfel MR. Evaluation of nonresponse bias in a cohort study of world trade center terrorist attack survivors. *BMC Res Notes*. 2015;8:1–11.