

WTC Health Program -- Petition 020

Summary of studies containing limited findings regarding an association between 9/11 exposure and stroke

The literature review conducted in response to Petition 020 requesting the addition of “two forms of stroke, both ischemic and non-aneurysmal hemorrhagic,” to the List of WTC-Related Health Conditions identified 12 studies appearing to potentially meet the WTC Health Program’s criteria for further evaluation. Three of those 12 studies were fully evaluated in the Program’s review of Petition 020, however, 9 of the 12 studies were found to not meet the Program’s criteria for further consideration. Five of the 9 studies not meeting the Program criteria were not further considered. However, because four of the studies referenced stroke in 9/11-exposed or potentially exposed populations, including limited findings regarding an association between 9/11 exposure and stroke, the Program determined that an explanation for why these studies are not considered peer-reviewed, published, epidemiologic studies of stroke in the 9/11 population is warranted. The four studies were ultimately determined inappropriate for full evaluation because they did not specifically evaluate the association between 9/11 exposure and stroke such that the Program could conduct the necessary analysis. The findings of the four studies are briefly discussed here to illustrate their inability to provide dispositive information about an association between 9/11 exposure and stroke: Lin *et al.* [2010],¹ Jordan *et al.* [2013],² Wilkenfeld *et al.* [2016],³ and Li *et al.* [2018].⁴

¹ Lin S, Gomez MI, Gensburg L, Liu W, Hwang SA [2010], *Respiratory and Cardiovascular Hospitalizations after the World Trade Center Disaster*, Arch Environ Occup Health 65:12-20.

² Jordan HT, Stellman SD, Morabia A, Miller-Archie SA, Alper H, Laskaris Z, Brackbill RM, Cone JE [2013], *Cardiovascular Disease Hospitalizations in Relation to Exposure to the September 11, 2001 World Trade Center Disaster and Posttraumatic Stress Disorder*, J Am Heart Assoc 2(5):e000431.

³ Wilkenfeld M, Fazzari M, Segelnick J, Stecker M [2016], *Neuropathic Symptoms in World Trade Center Disaster Survivors and Responders*, J Occup Environ Med 58:83-86.

⁴ Li, J, Zweig KC, Brackbill RM, Farfel MR, Cone JE [2018], *Comorbidity Amplifies the Effects of Post-9/11 Posttraumatic Stress Disorder Trajectories on Health-Related Quality of Life*, Qual Life Res 27:651-660.

1. Lin *et al.* conducted an ecological study designed to examine whether hospital admissions increased after September 11, 2001 due to respiratory and cardiovascular illnesses (including cerebrovascular diseases).⁵ The study used data from the New York State Department of Health's, Statewide Planning and Research Cooperative System (SPARCS) to compare hospital admissions among residents living near Ground Zero in lower Manhattan (affected area) to those living in an area of Queens (control area) during the same time period, and to compare admissions before and after September 11, 2001 among residents in lower Manhattan. The study found that the baseline hospital admission rate for all cardiovascular diseases combined was significantly lower in the affected area before September 11, 2001. The rate of hospital admissions specifically related to cerebrovascular disease in the affected area increased significantly during the weeks following September 11, 2001 as compared with the previous 10 years; a comparison of the cerebrovascular disease-related admission rates in lower Manhattan to those in Queens during the same time period, however, showed no statistically significant difference. The main limitation of Lin *et al.* is the ecological design, which measured exposure and hospital admissions at the group level, rather than in individuals. Ecologic studies are prone to concluding that because an association exists between exposure and a health outcome at the group level, it therefore exists at the individual level. Because the study did not evaluate the exposed population at the individual level, did not report on stroke independently from other cerebrovascular diseases, did not examine hospital admissions after 2001, and did not control for

⁵ Cardiovascular disease includes chronic rheumatic heart disease, hypertension, acute coronary artery disease (CAD), chronic CAD, cardiac dysrhythmia, congestive heart failure, and cerebrovascular disease. Cerebrovascular disease, a subcategory of cardiovascular disease, includes ischemic stroke, non-aneurysmal hemorrhagic stroke, aneurysmal subarachnoid hemorrhage, other and unspecified intracranial hemorrhage (e.g. subdural hemorrhage), transient ischemic attack, acute but ill-defined cerebrovascular disease, other and ill-defined cerebrovascular disease (e.g. hypertensive encephalopathy, cerebral arteritis, unruptured cerebral aneurysm), and late effects of cerebrovascular disease (e.g. speech and language deficits, hemiplegia/hemiparesis).

possible confounding factors and biases, the Program could not conduct the Bradford Hill evaluation of the study's findings necessary to support the addition of stroke to the List.

2. Jordan *et al.* conducted a cohort study designed to determine whether 9/11 exposures were associated with an increased risk of subsequent cardiovascular and cerebrovascular disease hospitalizations. The study matched data from 46,346 WTC Health Registry members who reported no incidence of post-traumatic stress disorder (PTSD) prior to September 11, 2001, with data from the New York State SPARCS database to identify individuals who were hospitalized for cardiovascular disease between the date of Registry enrollment and December 31, 2010. Data obtained from the Registry were self-reported; rescue and recovery workers were analyzed separately from survivors, and each group was placed into either low, intermediate, or high exposure categories. The study found that male enrollees who had PTSD at study enrollment (between September 12, 2003 and November 24, 2004) had an increased risk for cerebrovascular disease hospitalization [adjusted hazard ratio (aHR) = 1.5, 95% CI 1.0-2.3]; risk for cerebrovascular disease hospitalization among female enrollees who had PTSD at study enrollment was non-significantly elevated [aHR = 1.4, 95% CI 0.9-2.1]. Jordan *et al.* adjusted for race/ethnicity, education, marital status, smoking, and history of diabetes and hypertension, however it was unable to evaluate family history and dyslipidemia. Ultimately, the authors "did not determine whether PTSD was part of the causal pathway between 9/11-related environmental exposures and [cardiovascular disease, including stroke] hospitalizations or whether PTSD and rescue/recovery-related exposures were independent risk factors." Because stroke was grouped with other cerebrovascular diseases and not evaluated *per se*, Jordan *et al.* was not included in the Bradford Hill analysis described in the accompanying *Federal Register* notice.

3. Wilkenfeld *et al.* conducted a cross-sectional study designed to investigate whether the prevalence of neuropathic symptoms was greater among the 9/11-exposed population than the non-9/11-exposed population.⁶ A five-part survey was distributed to responders and survivors through the FealGood Foundation, faculty and staff at Queens College, Winthrop University's Occupational/Environmental Medicine Division, and health facilities associated with Winthrop University. The survey included questions about 9/11 exposure, including whether the respondent had been caught in the WTC dust cloud and whether he or she worked on the pile at Ground Zero, and for how long. Respondents also answered survey questions about medical comorbidities, including stroke. The authors compared the frequency of stroke among 9/11-exposed and non-9/11-exposed cohorts, finding no statistically significant differences between the two groups ($P=0.52$). This study did not evaluate the association between 9/11 exposures and the risk of stroke, nor did it determine whether reported strokes occurred before or after individuals' 9/11 exposures; therefore, Wilkenfeld *et al.* was not further considered by the Program.

4. Li *et al.* examined the burden and impact of physical and mental comorbidities on the health-related quality of life among WTC Health Registry members with 9/11-related PTSD. Post-9/11 PTSD trajectory was assessed using the PTSD Checklist (specific);⁷ study subjects were categorized into four groups – chronic, delayed, remitted, and no PTSD. Physical comorbidities were self-reported, and included respiratory diseases, cardiovascular diseases (including stroke), autoimmune and endocrine diseases, gastroesophageal reflux disease, and

⁶ Neuropathic symptoms were measured by use of the Michigan Neuropathy Screening Instrument. Examples of neuropathic symptoms include but are not limited to numbness, burning pain, and cramps in legs and/or feet; ulcers; and temperature insensitivity. See http://www.med.umich.edu/borc/profs/documents/svi/MNSI_patient.pdf.

⁷ See <https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp>.

sarcoidosis. The study found that the age-adjusted prevalence of cardiovascular disease, including stroke, was highest for those with chronic PTSD, followed by delayed PTSD, remitted PTSD, and the lowest for those with no PTSD. The prevalence ratio of chronic to no-PTSD groups for stroke was 2.3 (no significance testing was provided). Because participants lost to follow-up were likely healthier than those who chose to stay in the study, the findings in Li *et al.* were subject to selection bias, potentially distorting the study results. Ultimately, although Li *et al.* offered insight into the relationship between WTC-related PTSD and stroke, it was of limited value and was not included in the Bradford Hill analysis because it did not evaluate the association between 9/11 exposures and stroke.