American Thoracic Society

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John J. Howard, MD
Administrator
World Trade Center Health Program
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
Via Regulations.gov submission

Re: NIOSH Docket #334, CDC-2020-0035
World Trade Center Health Program Research Agenda

Dear Dr. Howard:

On behalf of the American Thoracic Society (ATS), thank you for the opportunity to provide comments on the 2021 World Trade Center Health Program Research Agenda. The ATS looks forward to working with the National Institute for Occupational Safety and Health (NIOSH) to further develop and implement this plan and provide expert peer review of grant applications. We have the following comments and recommendations:

World Trade Center (WTC) rescue and recovery workers and survivors have a high burden of chronic health conditions (CHC) associated with WTC-exposures.[1] Such CHC include upper and lower respiratory conditions (asthma, COPD, chronic rhino-sinusitis), GERD, mental health disease such as post-traumatic stress syndrome (PTSD), cardiovascular disease/risk factors and neurocognitive decline, and each of them is associated with reduced quality of life and sleep quality.[2,3]

Most recently, a high risk for cancer incidence, particularly of the head and neck, thyroid and prostate has been consistently reported across several WTC cohorts.[4] Because asbestos was used for insulation when the WTC towers were built, there is also concern that anyone within a 1.5 mile radius of the WTC was at risk for asbestos exposure. An increase in reported cases of mesothelioma is thus expected to emerge in the near future, given twenty to fifty-year latency. Furthermore, cardiovascular disease and risk factors have been identified as WTC-associated CHC. Specifically, classic cardiovascular risk factors such as metabolic syndrome have been identified as risks of WTC-Lung Injury and WTC-Airway Hyperreactivity.[5-13]

The known progression of CHC in the WTC cohort and increased cancer incidence decades after the original exposure raises concern for unrecognized cardiovascular risk, sleep disturbance and

disease. Metabolic syndrome affects at least 30 % of the WTC-exposed population.[7,11-13] There is recent literature that metabolically active pathways are relevant to the development of WTC-lung disease in murine models and that inhibition of these pathways are protective.[14-16]

Notably, the prevalence of obstructive sleep apnea (OSA), through questionnaire or objective testing, is as high as 60-80%, much higher than observed in other epidemiologic cohorts with similar characteristics, and in middle-aged general, non-WTC populations.[17-21] In turn, untreated OSA is a well-established risk for cardiovascular, cerebrovascular and neurocognitive/neurodegenerative morbidity and mortality.[22,23] [24,25] Additionally, in patients with PTSD, coexistent sleep disturbance/insomnia and OSA worsen PTSD symptoms, quality of life and adversely impact response to PTSD treatment.[26]

Research Recommendations

The WTC cohort is an appropriate group for research inquiries into the aforementioned interactions. Given the specific morbidities and risks of this cohort, the ATS recommends that the World Trade Center Health Program research agenda include the following research priorities:

1. Continued research on pulmonary diseases such as asthma/COPD, and lung cancer, with exploration of other areas such as interstitial lung disease, granulomatous lung disease, asbestosis, and mesothelioma risk
2. Studying the effects of PTSD on both airway disease and sleep disorders
3. Continued assessment of the association of 9/11 exposure to morbidities such as multisystem or autoimmune, cardiovascular and neurologic diseases
4. Further assessing changes in the health of children that were exposed on 9/11
5. Characterizing established WTC-related diseases and comorbidities to identify phenotypes, epigenetic mechanisms, and omics biomarkers
6. Determining cardiopulmonary risk phenotype in WTC- exposed populations (e.g., omic and clinical biomarkers)
7. Characterize pathways involved in WTC associated cardiopulmonary disease; further develop murine models of WTC-Associated CHC such as lung injury, airway hyperreactivity
8. Study of phenotypes/mechanisms of sleep disturbance insomnia and OSA in this cohort, and their roles in predicting incidence of related disease (cancer, mental health issues, cancer), adherence and response to treatment modalities for sleep disturbance and OSA

9. Determine how WTC-exposure and metabolic derangement interact to potentiate disease development of WTC associated lung and vascular disease
10. Exploration of the role of WTC exposures in increasing the risk for upper airway cancers

Again, we thank you for the opportunity to provide feedback. We look forward to further assisting the WTC Program with specific research priorities and any other information. Please contact Nuala S. Moore, Director of Government Relations with any questions or for more information at Nmoore@thoracic.org.

Sincerely,

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President
American Thoracic Society

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