HHS Public Access

Author manuscript

Am J Ind Med. Author manuscript; available in PMC 2022 November 03.

Published in final edited form as:

Am J Ind Med. 2021 October ; 64(10): 797–802. doi:10.1002/ajim.23273.

The World Trade Center Health Program: Twenty years of health effects research

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Abstract

It has been 20 years since the devastating terrorist attacks on September 11, 2001. Thousands were injured or killed during the attacks and many more are at risk of adverse health stemming from physical, psychological, and emotional stressors born out of the attacks. Private, federal, state, and local resources were gathered soon after the attacks to address impacts to the community, including the health and well-being of both responders and survivors. Many of these efforts are now largely consolidated under the federally mandated World Trade Center (WTC) Health Program. This program provides medical monitoring and treatment of qualifying conditions among the 9/11-exposed population and supports related physical and mental health research. In this commentary, we describe the WTC Health Program, with emphasis on the health-effects research it has funded since inception in 2011. We describe sentinel research publications, and

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AUTHOR CONTRIBUTIONS

Robert D. Daniels participated in all aspects of the work, including conception, interpretation, writing, and critical revisions for important intellectual content, final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Travis L. Kubale, Dori B. Reissman, and John Howard participated in critical revisions for important intellectual content, final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interests.

DISCLOSURE BY AJIM EDITOR OF RECORD

Steven Markowitz declares that he has no conflict of interest in the review and publication decision regarding this article.

ETHICS APPROVAL AND INFORMED CONSENT

This study was conducted by US government employees of the National Institute for Occupational Safety and Health, which is part of the Centers for Disease Control and Prevention (CDC) under the United States Department of Health and Human Services. No contact was made with study participants. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy. This activity does not constitute human subjects research as defined by 45 CFR §102(I). Ethics review and approval and informed consent was not required.

DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

how science has impacted the program. We provide examples relating studies in this special issue to important roles in the WTC Health Program research agenda. Finally, we provide a perspective on future research needs.

1 | INTRODUCTION

As we approach the 20th anniversary of the 9/11 terrorist attacks, we are once again reminded of the thousands who lost their lives or were injured that day. We also grieve for many more who now suffer from adverse health effects stemming from the physical, psychological, and emotional stressors born out of the attacks. The health of nearly a half million people is potentially at risk from exposures attributable to 9/11.[1] In the aftermath of the attacks, private, federal, state, and local resources supported several postdisaster activities, including recovery actions, the World Trade Center (WTC) Health Registry, and caring for the affected population in several surrounding health-care facilities. Health-care activities were later consolidated with the passing of the James Zadroga 9/11 Health and Compensation Act of 2010 (The Act), establishing the WTC Health Program[*1]. The WTC Health Program is a limited health benefits program for qualifying health conditions related to the 9/11 attacks and aftermath. It provides medical monitoring and treatment of eligible responders, initial health evaluations for eligible survivors, and medical monitoring treatment for survivors who have health conditions certified by the Program. The Program resides under the U.S. Department of Health and Human Services and is administered by the Director, National Institute for Occupational Safety and Health (NIOSH). There are currently over 100,000 persons enrolled in the Program (https://www.cdc.gov/wtc/ataglance.html).

Shortly following the attacks, several research groups in New York City (NYC), surrounding areas, and elsewhere, began characterizing impacts to response/recovery workers and the community, including detriments in physical and mental health among the exposed populations.[2-6] These efforts have continued over the last 20 years, and in 2011 were codified into The Act. The Act stipulates research on physical and mental health conditions that may be related to the attacks, as well as diagnosis and treatment of existing WTC-related health conditions. Research priorities are determined by the WTC Health Program with stakeholder input. Funding is provided through grants and cooperative agreements managed by the WTC Health Program in collaboration with the NIOSH Office of Extramural Programs through a National Institutes of Health framework for solicitation and competitive award. The available research is expansive, with nearly 1000 articles published in the peer-reviewed literature from 2001 to 2020.[7] The portfolio includes exposure science, toxicologic, and epidemiologic research from experimental and observational (analytic and descriptive) studies designs. Study endpoints are diverse, covering a broad range of physical and mental health conditions. Collectively, these studies contribute to the rich data needed to characterize and mitigate the evolving health burden in an aging population.

* [1]Title XXXIII of the Public Health Service Act as amended, 42 U.S.C. 300 mm to 300mm-61 (codifying Title I of the James Zadroga 9/11 Health and Compensation Act of 2010, Pub. L. 111-347, as amended by Pub. L. 114-113).

2 | IMPACTS FROM EXISTING RESEARCH

Consistent with The Act, the WTC Health Program research agenda examines a wide array of health conditions potentially linked to 9/11 exposures that are conveniently grouped into one of five categories, namely: aerodigestive disorders, mental health conditions, musculoskeletal disorders, cancers, and traumatic injuries. Although a research outcome of interest may at first glance fall into a particular category, most outcomes involve complex etiology and pathology that can involve multiple categories. For example, untreated chronic gastroesophageal reflux disease (an aerodigestive disorder) increases the risk of developing esophageal adenocarcinoma (a type of cancer). To illustrate the breadth and depth of the many research contributions to date, we have selected a few sentinel publications for discussion in this commentary.

2.1 | Aerodigestive disorders

Recall that both responders and survivors were exposed to intense levels of airborne hazardous substances (e.g., asbestos, silica, heavy metals, volatile organic compounds, and polyaromatic hydrocarbons) in gases and alkaline mixtures of coarse and fine particles that were produced by the fires and catastrophic collapse of buildings on 9/11, and were resuspended during recovery actions that followed.[8,9] Thus, research examining the risk of acute respiratory illnesses was at the forefront of early efforts examining health effects from the attacks. Among early influential studies, is the highly cited publication by Prezant et al. (2002) who first examined the clinical features of the “World Trade Center cough” observed among firefighters and rescue workers responding to the scene.[10] WTC cough is described as a persistent (and debilitating) cough, usually accompanied by other upper and lower respiratory symptoms such as nasal congestion, sinusitis, gastroesophageal reflux, dyspnea, and wheezing. In studying exposed responders, Prezant et al. (2002) observed that WTC cough occurred in about 8% of those present during the collapse and that their symptoms increased with exposure intensity.10

This study demonstrated for the first time that 9/11 exposures were associated with clinically diagnosed aerodigestive disorders, such as bronchial hyperresponsiveness and other severe respiratory disease. Aerodigestive disorders currently comprise the largest category of WTC-related conditions, accounting for over half (54%) of the certified conditions among WTC Health Program members enrolled through 2020. Nearly $37 M has been awarded for studies on WTC-related aerodigestive disorders, accounting for about 29% of the WTC Health Program research dollars spent between 2011 and 2020.[7]

2.2 | Mental health

The broad category of mental health research includes assessing disorders such as posttraumatic stress disorder (PTSD), major depressive disorders, panic disorder, and various anxiety disorders that are linked to the terrorist attacks. Nearly $26 M has been awarded by the WTC Health Program for mental health research between 2011 and 2020, accounting for 21% of the total funds awarded.[7] About 21% of certified conditions through 2020 fall into the category of mental health disorders.

Most of the mental health research focuses on PTSD, which can often result in marked disability and comorbidity among patients. This research has shown that although most appear resilient, PTSD symptomology can persist decades postexposure in a sizable subgroup of patients. For example, in a recent landmark study, Bromet et al. (2016) longitudinally examined a group of general responders (n = 3231) with complete information on PTSD, exposures, and loss of colleagues in the tower collapse.[11] The group comprised police (49%) and a heterogeneous subgroup of nontraditional responders (e.g., construction workers, electricians, transportation workers, and utility workers). They examined trajectories of PTSD symptoms using monitoring data collected from observations on average intervals of 1.6 years (23,086 person-years). They reported that nearly 20% of all responders were diagnosed with WTC-related PTSD. Nontraditional responders were twice as likely to develop WTC-related PTSD compared with police; this was attributed to differences in experience and disaster preparedness. Among those ever diagnosed with PTSD, about half had active disorder at time of last interview, occurring 11–13 years postexposure. Avoidance and hyperarousal symptoms were most frequent among those with active PTSD. Exposures to the 9/11 dust cloud, human remains, injury, or death were strongly predictive of both active and remitted PTSD. WTC-related PTSD risk was also strongly associated with self-reported poor physical health and life dissatisfaction. These findings suggest increased vigilance in surveillance and research to address interactions between mental, physical, and social well-being among WTC Health Program members.

2.3 | Cancer

Exposures to several known or suspected carcinogens (e.g., dioxins, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, benzene, cadmium, and asbestos) immediately prompted concerns of excess cancer.[8,9,12-14] Zeig-Owens et al. (2011) published the first longitudinal study examining the association between cancer incidence and WTC exposures.[15] Their early assessment included nearly 10,000 male Fire Department of the City of New York fire-fighters who were followed for up to 7 years postexposure, observing 263 cancers among exposed firefighters. Zeig-Owens et al. (2011) reported modest excess cancer risk among the exposed group compared with the general population (standardized incidence ratio [SIR] = 1.10; 95% confidence interval [CI]: 0.98, 1.25).15 Among specific tumors examined, there was significant excess risk of melanoma (SIR = 1.54; 95% CI; 1.08, 2.18; n = 33), prostate cancer (SIR = 1.49; 95% CI: 1.20, 1.85; n = 90), thyroid cancer (SIR = 3.07; 95% CI: 1.86, 5.08; n = 17) and non-Hodgkin lymphoma (SIR = 1.58; 95% CI: 1.03, 2.42; n = 21). These findings helped define an evidence base for rulemaking in 2012–2014 adding cancers to the list of eligible conditions codified in The Act. Today, cancers account for about 24% of certified conditions among members. Cancer remains a major component of ongoing research, accounting for about 21% of the research funds awarded by the WTC Health Program, mostly for observational studies examining cancer incidence and mortality in both responder and survivor populations.[7] Collectively, these studies provide limited evidence of increased cancer risk, mostly for cancers of the thyroid and prostate, with inconsistent reports of excess bladder cancer, malignant melanoma, multiple myeloma, leukemia, and non-Hodgkin lymphoma across studies.[15-20] Future research will extend follow-up, resulting in a more thorough understanding of late-developing cancers, increased statistical power, and improved internal validity. In addition, studies that better elucidate

disease mechanisms and inform clinical care of current cancer patients are becoming increasingly important to the WTC Health Program research agenda.

2.4 | Emerging conditions (cognitive impairment)

As the at-risk population ages, research into persistent and late-emerging health effects are increasing in prominence. WTC Health Program research and surveillance programs have provided some preliminary evidence pointing to potential discovery of new associations between 9/11-exposures and chronic health conditions, such as autoimmune diseases,[21-23] cardiovascular disease,[24-30] and neurological disorders.[31-37] Continued research involving these emerging conditions and others is an integral part of the WTC-Health Program, including its important role in future changes to the list of qualifying health conditions.[38]

As an example of emerging conditions research, there is some evidence suggesting increased mild cognitive impairment among responders, now at midlife, that might be attributable to 9/11 exposures.[31-37] Clouston et al. (2016) was among the first to evaluate the association of PTSD and major depressive disorders with cognitive impairment in a sample of general responders.[34] Researchers screened participants for cognitive impairment and dementia using the Montreal Cognitive Assessment and found that nearly 13% of participants had scores suggesting cognitive impairment, and about 1.2% suggesting dementia. Using another instrument, a subsequent study examined the association between WTC inhalation exposures and overall cognitive dysfunction in responders.[32] That study found that nearly 15% of participants presented with cognitive dysfunction compared with aged-matched normative data, and that PTSD symptom severity and working more than 5 weeks on the recovery site were associated with lower cognition. This study group also conducted neuroimaging that indicated reduced whole-brain and regional cortical thickness in the entorhinal and temporal cortices in both the cognitively impaired and unimpaired responder groups compared with published normative data.[36] The pattern of reduced cortical thickness in exposed responders was largely dissimilar to known neurodegenerative diseases, which may point to a WTC-specific neuropathology. Still, there is much uncertainty in causal inference given key limitations in available observational studies.[35] More research is needed to characterize the burden of cognitive impairment in the 9/11-exposed population. Causal pathways remain unclear, including contributions that may be associated 9/11 exposures. Moreover, if a causal association exists, then it is still not clear whether impairment stems from progression of WTC-related chronic mental health disorders or is caused by airborne neurotoxins and fine particulates from 9/11 exposures, or both.[39-46]

The WTC Health Program, together with other leaders in cognitive research, held a scientific workshop to discuss the state of science, including the natural history of cognitive aging and impairment, biomarkers in the pathway of neurodegenerative diseases, the neuropathological changes associated with hazardous exposures, and the evidence of cognitive decline in the 9/11-exposed population.[35] Insights from the workshop were incorporated into the 2021 call for WTC Health Program research aimed to clarify burden, causal mechanisms, and targeted interventions that improve patient care.

3 | SPECIAL ISSUE: EXAMPLES OF NEW RESEARCH

This special issue also provides a unique glimpse into the research portfolio supporting the WTC Health Program. Included in this issue are studies of responder and survivor populations that examine existing and persistent conditions, emerging conditions, intervention effectiveness, and changes in quality of life measures over time.

For example, several chemicals in 9/11-dusts have been linked to liver disease and hepatic cancer in other studies. Moreover, research suggests an association between particulate exposures and metabolic syndrome, which may affect nonpulmonary organs, such as the liver.[47,48] Yet, few studies have examined liver disease in the 9/11-exposed population. Jirapatnakul et al. (2021) examined hepatic steatosis in a large group of general responders primarily involved in cleanup.[49] They found a statistically significant increasing trend in steatosis with arrival time on the pile, indicating a greater risk among those responding early compared with later arrivals. This study provides new evidence of an exposure-response relationship between hepatic steatosis and 9/11-dust exposure.

As an example of existing conditions, van Gerwen et al. (2021) discusses current and future research of thyroid cancer in the WTC population.[50] Some studies have indicated excess thyroid cancer, a disease with few known environmental risk factors, among the exposed population.[15,16,18,20] Some have posited that these results reflect heightened medical surveillance rather than exposure-related disease.[51] Still, others have argued against a strong surveillance bias that can fully explain findings of excess thyroid cancer risk.[52,53] Given this uncertainty, the authors discuss the need for more epidemiologic research to clarify the potential for bias and to develop methods that appropriately address uncertainty in future cancer research. In the presence of a true causal association between 9/11 exposure and thyroid cancer, the authors point to a need for toxicologic studies that elucidate mechanisms of WTC-related thyroid cancer. This study may shape future risk mitigation strategies in urban disasters.

As an intervention, Goldfarb et al. (2021) compared survival among cancer patients in three groups: responders enrolled in medical monitoring and treatment programs in New York City (NYC, the treatment group); responders who do not participate in the NYC programs; and New York State cancer patients who are not in the responder group.[54] Survival was improved among the treatment group compared with either control group after adjusting for demographic factors and temporal trends. This suggests that participating in treatment offered at no-cost by the WTC Health Program may benefit survival among cancer patients.

Given an aging population, the need for research involving circulatory system diseases (e.g., cardiovascular and cerebrovascular diseases) is steadily increasing. In this issue, Yu et al. (2021) examine the relationship between PTSD, dust exposure, and stroke in nearly 30,000 persons enrolled in the WTC Health Registry.[55] In dose–response models they found that 9/11 dust exposures were a possible risk factor for ischemic stroke, but not for hemorrhagic stroke. They also found association between PTSD and ischemic, hemorrhagic, and recurrent strokes. These findings appear consistent with a previous study first reporting associations between 9/11-related PTSD, intense dust exposure, and increased

risk of developing stroke.[27] Thus, this study adds to growing evidence of associations between cerebrovascular disease and 9/11 exposure, as well as information suggesting the risk of stroke may be mediated by PTSD, an existing WTC-related condition.

Finally, we have shown that some physical and mental health effects have persisted or are emerging late in life in several persons with 9/11 exposures. These effects may inhibit a person's ability to function at home or at work, which in turn can further diminish one's physical, mental, and financial well-being. For example, Seil et al. (in press) examined how 9/11-related injuries affected retirement patterns among enrollees in the WTC Health Registry.[56] They found that being injured on 9/11 was a predictor of earlier retirement and uninjured workers tended to continue working longer.

4 | FUTURE DIRECTIONS

As we enter the third decade since 9/11, we can reflect on the wealth of information that has originated from an extensive research program. This research has played important roles in identifying and characterizing WTC-related health conditions and in the treatment of these conditions. The research shown in this special issue is a sample of the most recent contributions to the literature serving the WTC Health Program. Findings from these studies answer key questions but also illuminate existing gaps, demonstrating an unrelenting and urgent need for continued research.

This commentary, and the other content of this special issue, touches the surface of the available research on WTC-related health effects. For more information, readers are encouraged to refer to the review by Santiago-Colon et al. (2020) who describe WTC research completed over the last 20 years.[7] Although much has been accomplished, many unanswered questions remain and many more will likely surface over time. Given that the WTC Health Program is authorized through 2090, etiologic and interventional research is foreseen well into the future. More is needed to elucidate knowledge gaps in causal effects, disease progression, and emerging health conditions. Program members will benefit from research targeting health equity among vulnerable subpopulations (e.g., persons exposed as children, elderly, and minority populations) and understudied outcomes (e.g., autoimmune diseases, cardiovascular, reproductive, and developmental endpoints). Finally, continuing research on WTC-related health conditions provides lessons learned that may reduce the risk of adverse health in populations affected by future disasters.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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