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Terms and Abbreviations

Abbreviation	Term
BRFSS	Behavioral Risk Fact Surveillance System
HWE	Healthy Worker Effect
NHANES	National Health and Nutrition Surveillance System
NHIS	National Health Interview Survey
NYC	New York City
PTSD	Posttraumatic Stress Disorder
RHC	Responders' Health Consortium
SES	Socioeconomic Status
SMR	Standardized Morbidity Ratio
UPI	United Press International
WTC	World Trade Center
WTC DC	Mount Sinai World Trade Center Data Center

Abstract

WTC responders' health status was evaluated using self-reported questionnaire data from the inception of the WTC Health Program to 2010. This project identified an elevated rate of asthma prevalence compared to the general population after adjusting for age and gender. To minimize the Healthy Worker Effect, which can erroneously infer that the exposed group is likely have a protective effect or no increased health effect when compared to unexposed group, the occupation of WTC responders was matched with the general population. This project also identified that WTC responders who developed new onset asthma after the WTC exposure were more likely to lose their full-time job status. There is no plausible biological explanation for a direct causal relationship between WTC exposure and lowered socioeconomic status. However, a secondary link was identified in which increased asthma incidence in our cohort was linked to lowered socioeconomic status among responders. This is an important finding which indicates that despite the lack of direct causative relationship, exposure to the WTC disaster can result in a reduction in SES for those exposed. Therefore, these findings are critical to consider when addressing their negative impacts for WTC responders. This project also found that new onset of probable rheumatoid arthritis has increased, which signals an association with WTC exposure may not be strong enough and has not been considered a WTC-related condition. Additionally, analysis showed a strong and clear protective effect on probable rheumatoid arthritis among those who used a respirator in the first week after 9/11. This finding suggests that personal level WTC exposure might be significantly different from group level exposure characteristics which have been used in WTC health research, such as time of arrival at the WTC site, duration of work, location of work, and tasks performed. Overall we were not able to conclude our findings with great confidence because of potential epidemiologic bias effects. Through the project, we identified several potential biases which can obscure the true association between WTC exposure and adverse health outcomes. It is important to evaluate the potential bias effects before concluding any of our findings. The bias analysis has been funded and currently in progress.

RESEARCH AIM/PROJECT OVERVIEW

Significant (Key) Findings

Specific Aims

Aim 1. Implement expanded occupational health surveillance of WTC responders

To accomplish this aim, WTC responders' questionnaire data from the inception of WTC responders' health consortium (RHC) 12/31/2010 were obtained from the Mount Sinai WTC Data Center (WTC DC). The list of datasets is presented in Appendix 1. Data quality such as possible errors were evaluated initially and then reported back to the WTC DC for confirmation and correction.

One of the main limitations of WTC health research among WTC responders is not having a comparison group (unexposed population). Without comparison to an unexposed group, the magnitude of adverse health problems among the exposed group (WTC responders) might not be properly estimated. In fact, most publications on WTC responders' health have been compared within the cohort and subsequently the strength of exposure and health outcome associations are weak or show no association. In this aim, to identify higher risk groups and properly detect emerging health outcomes, NHIS, NHANES and BRFSS were utilized and served as comparison groups. In epidemiologic research, the ideal comparison group would be created at the same time as the exposed group, both groups would be observed in an identical manner, and then the health outcomes would be compared at the end of observation. Unfortunately with this unprecedented tragedy t, creating a comparison group at the time of the earliest RHC (WTC Medical Screening Program) was not considered or feasible, given the rapidity of starting the WTC RHC. Therefore, we decided to utilize population surveys as comparison groups with matched health outcomes, measured by using the same wording of questions, such as "Have you ever diagnosed [type health condition]?". This method has several limitations such as only matched questions, matched study design (mostly cross-sectional), and matched study period (12 month or 24 month) could be used because general population surveys are not the ideal epidemiologic comparison group. However they were determined to be the best available method to measure the magnitude of health outcomes among WTC responders without the ideal comparison group. Details are presented in the appendix 2 and 6.

Using this method, annual prevalence and Standardized Morbidity Ratio (SMR) of five health outcomes (asthma, hypertension, diabetes, cancer, and stroke) which matched between two groups were calculated in the period of 2002-2010. National Health Interview Survey (NHIS), National Health and Nutrition Examination Survey (NHANES), and Behavioral Risk Factor Surveillance System (BRFSS) were used to obtain expected values in calculation of SMR (SMR=Observed value/Expected Value). Among the five health outcomes, after adjusting for age, gender and occupation, asthma was the only health outcome shown to exceed risk all the years since 9/11 compared to the general population with increasing trends over time (Appendix 2).

For mental health, instead of using the general population surveys, we conducted meta-analysis for Posttraumatic Stress Disorder (PTSD), which has been reported as the most prevalent health outcome from the WTC disaster (Appendix 3). This analysis demonstrated significant positive associations between WTC exposures and probable PTSD. The strength of associations appeared to be lower among WTC responders as compared to civilians who were exposed to WTC exposures.

While conducting aim 1, we learned that four health outcomes in SMR were lower or slightly higher in later years than the general population. This can be interpreted as WTC responders are healthier even after matching occupation between two groups to minimize the potential Healthy Worker Effect. We began to suspect potential epidemiologic biases and identified some potential biases which can lead to incorrect causal inference by distorting the associations between WTC exposure and health outcome. To identify further and quantify the impact of biases and to adjust the bias effects, we developed a grant proposal to conduct a multiple bias analysis using probabilistic bias analysis technique (Appendix 4). This proposal was awarded and is currently in progress. The overall objective of this study is to assist WTC research and researchers by providing information on potential biases and methods to adjust the bias effects for more accurate causal inference.

Aim 2. Identify effect of error when outcomes that were collected from different wording of questions are compared

We asked a set of questions to WTC responders at the Queens WTC Health Program clinic on their visit. The question set contained several pairs of questions that are slightly different in wording between the WTC questionnaire and the general population surveys (NHIS, NHANES, BRFSS), however the questionnaires were basically asking for same health condition. We were not able to collect and store the data due to the Paperwork Reduction Act (Pub. L. No. 96-511, 94 Stat. 2812, codified at 44 U.S.C. §§ 3501–3521); however we recommend that the wording of questions in two groups should be identical for comparison. In particular, ascertainment of case and time-frame of the case occur must be identical.

Aim 3. Identify the ambi-directional effect modification between Socioeconomic Status (SES) and health in the WTC cohort

Through this aim, we identified a mediation effect of asthma in between WTC exposure and lowered SES instead of the ambi-directional effect modification (Appendix 5). The study showed that WTC responders who were diagnosed with asthma after 9/11 had a 24% greater risk of losing their full-time job than those without asthma. In addition, significantly, asthmatics were 86% more likely to become disabled and 40% more likely to retire. In the stratified analysis by asthma, among asthmatics, WTC exposures (occupation on 9/10/01 and location of work at the WTC site in September 2001) showed significant association with losing their full-time job, while among non-asthmatics, none of the WTC exposures showed association with losing their full-time job. This analysis proved that SES is an important adverse consequence of WTC exposure through meditator (indirect association). Based on this study, we are planning additional analyses with various potential mediators including injury, physical health outcomes, and mental health outcomes.

TRANSLATION OF RESEARCH FINDINGS

From the SMR analysis (aim 1) where we compared WTC responders' five health outcomes (asthma, hypertension, diabetes, cancer, and stroke) to the general population, we found that WTC responders were generally healthier than the general population, except for asthma, for the entire period from 2002-2010. However the 12-month prevalence of all five health outcomes has been increasing gradually over the same time period.

The healthier trend of WTC responders versus the general population may be explained by the healthy worker effect (HWE), which may be that either healthier people were included in the exposed group or healthier people survived more often or longer, so the exposed group becomes healthier than the unexposed group. HWE can be minimized by matching occupation between exposed and unexposed groups. During our SMR analysis we also performed occupation matching and the healthier trend among WTC responders was still observed. This could be interpreted as HWE is not likely, or even healthier people within the same occupational group responded and worked at the WTC site. Or there may be some epidemiologic bias effects that have not been addressed. Therefore before concluding that healthier workers responded to WTC even in the same occupation and those who responded are still healthier than the unexposed population even after WTC exposures, we decided to conduct bias analysis for the potential effect that may explain the strange healthier trend. As a result, we were awarded another U01 grant (U01 OH010730-01) to conduct the bias analysis. This project proposed three aims with 1) biases identification, 2) bias effect quantification and adjustment, and 3) bias adjustment guideline development for future disaster studies. With completion of this project, the existence of epidemiologic biases will be identified and the methods to adjust the bias effect will be provided. This project will also explain the weak association between WTC exposures and health outcomes among WTC responders.

From aim 2, we confirmed that only matched questions between WTC questionnaires and NHANES, NHIS, and BRFSS should be compared and not perfectly matched questions should not be considered to compare between exposed and non-exposed groups. We recommend that future disaster studies consider using perfectly matched questions from standardized questionnaires without any modification in terms of exact wording and time window of health conditions or symptom occurred. This is particularly important in disaster epidemiology which often lacks the opportunity to build a comparison group due to the nature and unexpected occurrence of disasters. By using standardized questions without modifications, general population surveys can be used as a comparison group.

Aim 3, SES and health outcomes, confirms that WTC responders who developed asthma had a 24% greater risk of losing their full-time job than those without developing asthma. Moreover, asthmatics were 86% more likely to become disabled and 40% more likely to retire. Causal inference with multivariable regression modelling showed that among non-asthmatics, no WTC exposure variables were associated with losing their full-time job, while all previously reported demographic risk factors (gender, race, education, income, age, and 9/10 occupation) were associated with losing their full-time job. However among asthmatics, none of those demographic risk factors showed any association, while occupation and location of work at the WTC site were strongly associated (Relative risk (RR)=0.3 (95% CI=0.1-0.7)) for 9/10 occupation and RR=2.2 (95% CI=1.3-3.8)) for location of work). This is strong evidence that WTC responders had experienced losing their full-time job most likely from WTC exposures, and other demographic factors less likely play a role. This finding concludes that lowered SES among WTC responders with developing asthma is likely due to WTC exposures via asthma, and lowered SES should be considered as an important adverse consequence of WTC exposure. Currently we are planning mediation analysis with other various health outcomes to prove the same causal pattern between WTC exposures and lowered SES.

PUBLIC HEALTH RELEVANCE AND IMPACT

This project relates to occupational safety and health by identifying the unique exposures WTC responders experienced during this disaster, whether they persisted, and how we can better prepare for future catastrophic events.

The findings of this study can guide future investigations and research by:

- Providing methods to conduct epidemiologic causal inference for disaster cohort by utilizing general population surveys serving as unexposed/comparison group. It is common to fail creating a comparison group in disaster epidemiology especially with man-made disasters, which are hardly predictable. This project suggests utilizing questions from standardized questionnaires used by general population surveys such as NHIS, NHANES, and BRFSS, and matching occupation in order to minimize HWE.

- Epidemiologic biases can be a serious problem in accurate causal inference of disaster effect. Avoiding and controlling these biases are usually viewed as the overall goal of epidemiology. Particularly with the WTC health studies, we identified various potential biases. The WTC bias study proposal (Appendix 4) described potential biases from this cohort in detail. Due to the potential biases effect, we recommend WTC studies to identify and adjust those biases using probabilistic bias analysis or at least non-probabilistic bias analysis prior to making conclusions of associations.

- We found clear evidence of WTC effect on lowered SES by using loss of full-time employment status as an indicator among WTC responders who developed asthma. This mediation effect with asthma can be applicable to other health outcomes such as injury, other physical health, and mental health, and the magnitude of effect may vary. We are planning to expand this analysis with other health outcomes. We also recommend that other WTC cohorts conduct this mediation analysis to investigate lowered SES as a consequence of WTC exposure. The NYC WTC Health Registry already began conducting this analysis with Dr. Kim's collaboration.

- Beside the proposed aims, through the analysis, we identified and increased rate of probable rheumatoid arthritis among WTC responders. Analysis with a set of conventional WTC exposure variables including arrival time at the WTC site, duration of work at the site, location worked, and tasks performed, did not show a clear association with rheumatoid arthritis. However we identified using a respirator, both full and half face, in the first week of 9/11, had a strong protective effect (incidence rate ratio=0.66, 95% confidence interval=0.56-0.79) while mask use did not show a significant protective effect. This finding suggests: 1) respirators, not masks, should be provided to responders for the future disasters, and 2) the conventional exposure variables may not be measured accurately. If respirator use showed a clear association, then there must be exposures. Not showing associations with exposure variables that are supposed to predict a true quantity of exposure means that the variables may be misclassified, which can be a source of information bias.

PUBLICATIONS

Two peer-reviewed manuscripts published (Appendix 3 & 6) and three manuscripts are close to submission (Appendix 2, 5, 7). Findings were also presented at two international conferences, the Society for Epidemiologic Research (Appendix 8) and the International Congress on Occupational Health (Appendix 9) and four invited speaking events at the Midwest American Industrial Hygiene Association (2015), Stony Brook University (2014), New York City Department of Health and Mental Hygiene (2013), and University of Michigan (2013). The finding of increased asthma rate has been reported by numerous national and international sources including the United Press international (UPI).

APPENDICES

Appendix 1.

Documents included in Data Request for Hyun Kim (from Mount Sinai WTC Data Center)

Variable Maps

We only included the EAQ and longitudinal maps for the IAMQ and SAMHQ/Mental Health. In both the IAMQ and mental health datasets, the scope and nature of the questions asked changed in different versions within a visit. If you would like the variable maps to see changes within a visit we can provide them.

Visit 1 IAMQ – The scope and nature of the V1 IAMQ changed considerably between the Logician and Trialdb versions. This map outlines as clearly as possible which variables are present in the Logician questionnaire and which ones are present in the TrialdB questionnaire.

Longitudinal IAMQ

Longitudinal SAMHQ

Data Dictionary

This file outlines all of the variables that are in each dataset as well as which formats are attached to which variables. Each tab denotes a different dataset.
A second tab denotes different missing values and their meanings. For example, .M means that the information was missing for that question while a .N means that the question was not asked due to a skip pattern.

Format Inventory

This file includes an outline of all formats which are included in the various datasets.

Datasets

Visit 1

EAQ – Exposure Assessment Questionnaire
MHSQ – Mental Health Screening Questionnaire
PE – Physical Exam
There are some variables which were dropped in this dataset that are only present in some versions of the paper form. If you would like us to send those variables we can.
Logician IAMQ – Interviewer Administered Medical Questionnaire when data was entered into Logician (prior to 2010)
TrialdB IAMQ – Interviewer Administered Medical Questionnaire when data started to be entered into TrialdB starting in 2010.
PFT – Pulmonary Function Test

Visit 2

PE – Physical Exam
There are some variables which were dropped in this dataset that are only present in some versions of the paper form. If you would like us to send those variables we can.
IAMQ – Interviewer Administered Medical Questionnaire

SAMHQ – Self Administered Mental Health Questionnaire
There are some questions that were dropped from this dataset that are only asked in a couple of the intermediate versions of the questionnaire. If you would like them we can provide these variables.
PFT – Pulmonary Function Test

Visit 3
PE – Physical Exam
IAMQ – Interviewer Administered Medical Questionnaire
SAMHQ – Self Administered Mental Health Questionnaire
PFT – Pulmonary Function Test

Visit 4
PE – Physical Exam
IAMQ – Interviewer Administered Medical Questionnaire
SAMHQ – Self Administered Mental Health Questionnaire
PFT – Pulmonary Function Test

Visit 5
PE – Physical Exam
IAMQ – Interviewer Administered Medical Questionnaire
SAMHQ – Self Administered Mental Health Questionnaire
PFT – Pulmonary Function Test

Visit 6
PE – Physical Exam
IAMQ – Interviewer Administered Medical Questionnaire
SAMHQ – Self Administered Mental Health Questionnaire
PFT – Pulmonary Function Test

Visit 7
PE – Physical Exam
IAMQ – Interviewer Administered Medical Questionnaire
SAMHQ – Self Administered Mental Health Questionnaire
PFT – Pulmonary Function Test

Demographics
Includes all demographics as well as visit dates, consent status and clinic for each visit.

PFT- Visits 1-7
Visit 1 includes both pre and post datasets separately
Visit 2-7 includes just the pre datasets only
IAMQ_13 Variables
Smoking Questions
IAMQ_13A_## in Visit 2+. The combination of the two variables for visit 1(IAMQ_73_01, IAMQ_73_03) and the two variables in Visit 2 (IAMQ_13A_01_01,IAMQ_13A_03_01) allowed us to determine the patient's smoking status (current smoker, former smoker, never smoker). Smoking status is longitudinal. Cigar/Pipe questions were combined in Visit 1 to correspond with Visit 2 on questions. Other than Ever regularly smoked pipes/cigars and currently smoke pipes/cigars, smoking questions are not able to be investigated between Visits 1 and 2.
Drinking Questions

IAMQ_13B_## in Visit 2+. Other than number of drinks per beer, wine and hard liquor respectively, these questions are not able to be looked at between visits 1 and Visit 2+. While both Visit 1 and Visit 2+ ask about current drinking status, the response options differ greatly between the two versions.
Family Medical History
IAMQ_13C_## in Visit 2+. These questions only started being asked in Visit 2+.

Web app data
Numdays1-numdays7, I calculated the visit date (variable= visit Time) in the web app within 30 days of the vis1dt-vis7dt dates and kept all records within 30 days. If not you can select numdays=0 which means visit date in web app matches the vis1dt-vis7dt in the demographics file.
All records have been run against the consents from the frozen demographic file

Appendix 2

TITLE
Standardized Morbidity Ratios for Five Chronic Health Conditions Among World Trade Center Responders: Comparison with National Health Interview Survey

Authors: TBN

ABSTRACT
We evaluated the overall health status of WTC responders by comparing prevalence of five major health outcomes with that of the general population as represented by the National Health Interview Survey (NHIS). Potential associations between new onset of asthma and WTC exposures were also investigated, especially the effects of respirator use during rescue and recovery efforts.

A total of 25,787 participants in the WTC Health Program (WTCHP) Responder Health Consortium (RHC) from 2002 to 2010 were included in the analysis. To compare this cohort with the external NHIS population, standardized morbidity ratios (SMRs) for asthma, cancer, diabetes, hypertension, and stroke were calculated with adjustment for age and occupation separately, stratifying by gender in each case. Lifetime prevalence of each outcome was based on self-report. Focusing on asthma, internal comparisons of WTC exposure effects were modeled by incidence rate ratios (IRRs), obtained by Poisson (log linear) regression with generalized estimating equations and a robust variance structure designed to facilitate overdispersion.

Relative to the NHIS population, with adjustment for age, asthma showed moderate to high SMRs (range 1.3–2.8) in both genders throughout the nine-year follow-up period. Hypertension SMRs were mildly elevated (~1.1) among men after 2006. SMRs for diabetes were significantly lower than expected overall. Among men, cancer SMRs were initially lower, then rose toward 1 over the course of follow-up. Those for women showed a similar pattern with lower precision due to small counts. Stroke was surveyed only from 2004–2010, and yielded significantly lower SMRs throughout that time frame. Occupation-adjusted SMRs showed greater variation but similar trends to the age-adjusted versions, with asthma higher than expected per NHIS. Internally comparing WTC occupations with construction workers as the referent, elevated incidence of asthma was found for protective service (IRR = 1.31; 95% CI 1.12–1.54) and utility workers (IRR = 1.39; 95% CI 1.11–1.73). Comparing exposures with those responders who arrived on 9/11 in the dust cloud, those who arrived that day but avoided the dust cloud had a lower risk of asthma (IRR = 0.81; 95% CI 0.71–0.93). Notably, responders who used a half- or full-face respirator during the first week showed significantly lower risk (IRR = 0.70; 95% CI 0.60–0.82) than those without a respirator.

We found that asthma was the main health problem among WTC responders, and identified trends in cancer, hypertension, and stroke that warrant further analysis and continued follow-up of WTC responders. We also found an apparent protective effect against asthma with respirator use. This is an

important finding not only for the future disaster preparedness but also for protecting general workers from daily occupational exposure.

INTRODUCTION

Early exposure assessments of the World Trade Center (WTC) disaster yielded a wide range of hazardous substances for first responders and community residents. The consequences of these exposures for responders' health in particular may vary widely as well, considering their proximity and extended interaction with the many sources of dust, chemicals, and products of combustion. Asthma and other respiratory diseases have been linked to WTC exposure (Lin, et al, 2005; Herbert, et al, 2006; Brackbill, et al, 2006; Brackbill, et al, 2009; Wisnivesky, et al, 2011; Kim, et al, 2012; Brackbill, et al 2014). While cancer may be subclinical for years, monitoring commenced soon after the disaster, and associations have been reported (Moline, et al, 2006; Brackbill, et al, 2006; Perera, et al, 2007; Moline, et al, 2009; Solan, et al, 2013). Diabetes, hypertension, and stroke have also drawn attention (Brackbill, et al, 2006; Jordan, et al, 2013; Miller-Archie, et al, 2014). To our knowledge, there have been no studies comparing all of these chronic health conditions of responders.

While estimating WTC exposure-health effects associations, several of these previous studies used internal cohorts for comparison, e.g., exposed vs. unexposed to the dust cloud (Herbert, et al, 2006; Brackbill, et al, 2014). Internal comparisons are favored by some for mortality studies (Card, et al, 2006), and provide insulation from healthy worker effect (Checkoway, et al, 2004). Nonetheless, for WTC studies of health effects, accurate exposure measurement is challenging because subjects may recall their exposure histories inaccurately and/or choose to participate in a study due to their exposure (i.e., selection bias). Recognizing these obstacles, Svendsen, et al (2012) cite the use of external referents as a "lesson learned" from the WTC disaster.

The present article uses both external and internal comparison groups to assess health effects of WTC exposures over nine years following 9/11 for five chronic health conditions: asthma, cancer, diabetes, hypertension, and stroke. We analyzed surveys administered from 2002 through 2010 by the Responder Health Consortium (RHC) of the WTC Health Program (Moline, et al, 2008), and for external comparison, the annual National Health Interview Survey (NHIS; National Center for Health Statistics, 2015) spanning the same time period.

METHODS

The study cohort consisted of 25,787 WTC responders who participated in the RHC WTC Health Program between July 16, 2002 and December 31, 2010, and consented to have their information used for research purposes. Details regarding eligibility criteria have been published elsewhere (Herbert, et al, 2006). Participants underwent a comprehensive baseline interview and then were followed every 12–18 months with periodic interviews and exams, where they were asked about each of the five health conditions. RHC participation rates are shown in Table 4.

Our external comparison group was the NHIS, a stratified, multistage, probability cluster sample of US households (National Center for Health Statistics, 2015). This national survey provided the source of expected prevalence of each health condition in the general US population from 2002 to 2010 (Pleis and Barnes, 2008). NHIS has a cross-sectional design with a different sample of responders sampled yearly; sampling and interviewing are continuous throughout each year. The NHIS consists of interview-administered questionnaires that collect self-reports of symptoms and illnesses.

Health Conditions

The five health conditions—asthma, cancer, diabetes, hypertension, and stroke—were selected due to their similar representation in both surveys as well as their implication in previous reports (Lin, et al, 2005; Herbert, et al, 2006; Moline, et al, 2006; Brackbill, et al, 2006; Perera, et al, 2007; Brackbill, et al, 2009; Moline, et al, 2009; Wisnivesky, et al, 2011; Kim, et al, 2012; Jordan, et al, 2013; Solan, et al, 2013; Brackbill, et al 2014; Miller-Archie, et al, 2014). For each of these outcomes, corresponding items from both questionnaires appear in Table 1. Briefly, both surveys asked participants if they were ever diagnosed by a doctor as having any of the five conditions. For asthma, the RHC survey included history of reactive airways dysfunction syndrome. Lifetime prevalence for each health outcome included baseline and follow-up visits data.

WTC Dust Exposures

WTC exposures were also assessed using an interviewer-administered questionnaire. Among the various exposure variables collected, we selected four major WTC exposures that potentially indicate the level of WTC dust/fumes inhaled or absorbed. First, arrival time to WTC site, categorized as: (1) arrived on 9/11 in the dust cloud, (2) arrived on 9/11 not in the dust cloud, and (3) arrived on the 12th of September or later. Second, number of hours worked at WTC site in September, as a continuous variable. Third, location of work performed in September 2001, categorized as: (1) on the pile or in the pit, (2) adjacent to the pile or the pit, (3) landfill, (4) barges or loading piers, and (5) elsewhere, south of Canal Street or the Office of the Chief Medical Examiner at 520 First Avenue in Manhattan. These three dimensions of WTC exposure have previously been described in detail (Woskie 2011). Lastly, we included the type of respiratory protection equipment used during September 11–18 as three categories: (1) did not wear respiratory protective equipment, (2) nuisance dust/surgical/disposal masks, with a N95 to P100 rating at most, and (3) half-face or full-face respirator with replaceable filters/chemical cartridges/clean air supply (SCBA)/powered air purification (PAPR) (Antao, et al, 2011).

Demographics

For both RHC and NHIS, pre-9/11 occupations were identified by asking “what was your trade/profession on September 10, 2001?”. The free-text responses were cleaned and re-categorized using the Standard Occupational Classification (SOC) 2000 developed by the Bureau of Labor Statistics (BLS, 2015). Five major categories were used: (1) construction workers (SOC code: 47-000), (2) protective service workers (33-000), (3) electrical, telecommunications, & other installation & repair workers (49-000, abbreviated to “utility”), (4) Transportation and material movers (53-000, abbreviated to “transportation”) and (5) business, engineering & administration (11-000, 13-000, 17-000, abbreviated to “business”). Details of pre-9/11 occupation have been previously reported (Woskie, et al, 2011). Age at baseline visit was categorized as: 18–30, 31–40, 41–50, 51–60, and ≥61 years. Other potential confounders included in the comparisons of internal exposures were gender, race, ethnicity, education, income, marital status, and cigarette smoking. For exposure comparisons by adjustment of incident rate ratios (IRRs) from the RHC, race and ethnicity were categorized based on the Office of Management and Budget classification (Durch and Madans, 1997). However, in the NHIS, ‘‘Native Hawaiian/other Pacific Islander’’ and ‘‘American Indian/Alaskan Native’’ were coded to the ‘‘other race’’ category. This categorization was similarly applied to the RHC data. Smoking status was categorized into current, former, and never smokers.

Statistical Analyses

External Comparison: The X^2-test was used to compare the distribution of baseline characteristics of NHIS and WTC participants. Crude annual prevalences were calculated using NHIS sample weighting methods (NCHS, 2008). Age- and occupation-adjusted standardized morbidity ratios (SMRs) for each gender, as ratios of observed to expected counts, were calculated with a 95% confidence interval (CI) based on the Poisson distribution (Ulm, 1990). These SMRs were obtained by an indirect standardization method to determine expected counts from NHIS (Checkoway, et al, 2004).

Internal Comparison: For the internal comparison of exposure groups, person-time incidence rates for asthma were based on year of diagnosis. The risk of new-onset asthma was longitudinally compared using incidence rate ratios (IRRs) calculated by generalized estimating equation (GEE) regression with the Poisson distribution and a log link (Barros, 2003). To handle mild violations of the equidisperson assumption (underdispersion) of the Poisson distribution when the outcome variable is a binary or count response, the robust variance option in Stata was used (Cameron and Trivedi, 2009). Crude and adjusted IRRs were compared and an exploratory analysis to identify factors associated with respirator use was performed. Crude and adjusted prevalence ratios (PRs) were calculated to investigate demographic factors and WTC exposures as determinants of respirator use by a cross-sectional robust Poisson regression model with respirator use (yes/no) as the outcome.

All analyses were performed using Stata software version 11.2 (StataCorp LP). The study was approved by the Mount Sinai School of Medicine’s Institutional Review Board and the Institutional Review Board of the Feinstein Institute for Medical Research at the North Shore-LIJ Health System.

RESULTS

The distribution of demographics and other key characteristics of the RHC cohort are presented in Table 2, along with the prevalence of each health condition by cohort subgroup. The most commonly reported lifetime health conditions were hypertension (22.4%) and asthma (15.2%), whereas cancer, diabetes and stroke were less prevalent (all < 5%).

External Comparison

Age-adjusted SMRs over time, comparing the RHC cohort with NHIS for each of the five health conditions, by gender, are illustrated in Figure 1 [smr.x1.ps]. Compared to NHIS projections, responders of both genders showed significantly higher prevalence of asthma throughout follow-up, with generally increasing trends, with lifetime prevalences more than doubled by 2010 (2.57 and 2.82 for females and males, respectively). The responders reported less cancer over the first five years post 9/11, but appear to lose that protection in the last four years, where prevalence is roughly comparable to NHIS. Diabetes and stroke are lower than NHIS across all nine years, while hypertension ticks upward in the later years for both genders, significantly exceeding the NHIS referent among men, peaking at 1.17 (95% CI 1.13–1.22) in 2008.

An analogous display for occupation-adjusted SMRs appears in Figure 2 [smr.x1.occ.ps]. These SMRs exhibit roughly the same trends as their age-adjusted counterparts. Among females in 2002 there is a significantly high SMR for diabetes of 3.19 (95% CI 1.28–6.56), but this is based on only 7 cases out of 226 women, compared to an even lower NHIS prediction of 2.2.

Internal Comparison

Table 3 presents the incidence rate ratios for asthma, obtained by internal comparison of WTC exposure subgroups. Among reported pre-9/11 occupations, compared to construction workers, more asthma cases were reported by those in protective service (IRR = 1.31, 95% CI 1.12–1.54) and utility work (IRR = 1.39, 95% CI 1.11–1.73). Responders on 9/11 in the dust cloud around the WTC experienced more new-onset asthma than other exposure groups, defined by date of arrival or proximity to the WTC. The use of a half- or full-face respirator in the first week post-9/11 was indeed protective, providing a 30% lower incidence compared to no respirator (IRR = 0.70, 95% CI 0.60–0.82). Based on location of work, our results suggest that working adjacent to the pile/pit was worse than working directly on the pile/pit (IRR = 1.18, 95% CI 0.97–1.43).

DISCUSSION

We computed SMRs for five chronic health outcomes over nine years in responders exposed to the WTC disaster. Our comparison with NHIS shows that asthma continues to afflict this population, with prevalence rising through 2010. Since 9/11, upward trends in age-adjusted prevalence of cancer appeared for both genders, but almost all estimates are lower than predicted by NHIS. Hypertension exceeded its expected prevalence in men, with both genders showing increasing trends in this health condition. Information on stroke is sparse, and rates are well below that of the NHIS; however, both genders show increasing trends later in follow-up.

We also calculated asthma IRRs using four different dimensions of WTC exposure. The internal comparison indicates the benefit of a half- or full-face respirator in reducing asthma risk. For disaster preparedness, this highlights the importance of respirator availability, in addition to supporting their value to workers in general and the daily exposures they encounter.

Other studies have examined asthma using various WTC exposure groups and time frames. Within 16 months of 9/11, Lin, et al (2005) sent direct mail [n ≈ 3,000] to geographically distinct parts of Manhattan to gauge respiratory health effects of proximity to the WTC, and found increased associations for asthma in that time frame. Based on examination of responders in the RHC cohort through 2.6 years after 9/11 [n ≈ 9,000], Herbert, et al (2006) reported pulmonary function deficits via spirometry as well as other respiratory symptoms to be correlated with World Trade Center (WTC) exposures. Analysis of the first wave of interviews with survivors of damaged buildings [n ≈ 8,000] by the NYC WTC Health Registry (HR) revealed significantly high adjusted odds ratios (AORs) for asthma, comparing internal levels of exposure (Brackbill, et al, 2006). A wider selection from the HR cohort with longer follow-up [first two waves, n ≈ 46,000], including rescue/recovery workers and lower Manhattan residents, yielded elevated AORs for asthma with acute and prolonged exposure to the WTC site (Brackbill, et al, 2009). With additional enrollment and follow-up of the RHC cohort, Kim, et al (2012) found increasing rates of currently active asthma (any attack in previous 12 months) as well as lifetime asthma over 6.3 years post 9/11 [n ≈ 21,000], relative to annual NHIS rates, adjusting for age, gender, and other factors. Brackbill, et al (2014) described the impacts of WTC-related injury and the modifying effects of PTSD on chronic health conditions, including heart and respiratory disease (both significant), diabetes, and cancer, upon analysis of WTC HR data through early 2008. Higher cumulative incidence of asthma with increasing exposure was found in the RHC cohort through 2010 among rescue and recovery workers [n ≈ 27,000] by Wisnivesky, et al (2011).

Our report uses the same data as Wisnivesky, et al (2011), but compares the prevalence of asthma in the entire RHC cohort with external NHIS predictions. In the present study, we extended follow-up of asthma beyond that of Kim, et al (2012) to over nine years, and observed marked increases in prevalence through 2010, in both genders, using either age or occupation as the adjusting factor in the SMRs. The protective effect of a respirator is significant, where the internal comparison yielded an IRR of 0.70 (95% CI 0.60–0.82). This is consistent with the earlier findings of Wheeler, et al (2007), who examined the WTC HR cohort in the first three years after 9/11.

The threat of cancer was an immediate concern after 9/11 (Hitt, 2001). Carcinogens detected near the WTC include dioxins, polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), benzene, and asbestos (Moline, et al, 2006). In their study of survivors of damaged buildings, Brackbill, et al (2006) found insignificant elevations in cancer among exposed participants; however, that follow-up was only through Nov 2004, short of the typical dwell time for most cancer. In a longitudinal study of children born shortly after 9/11 to mothers residing near WTC, Perera, et al (2007) presented evidence of elevated exposure to PAHs in blood samples. A series of eight cases of multiple myeloma from the RHC cohort were described by Moline, et al (2009), with the distinction that four occurred in responders before the age of 45, which is unusual for this disease. In a later study of the RHC cohort restricted to the local four-state area, Solan, et al (2013) compared cancer incidence ratios with those from corresponding state tumor registries, and found significantly higher rates in the RHC for thyroid and prostate cancer. Based on additional accumulation of RHC data, our SMRs suggest increasing trends in cancer in both genders, when adjusted for age (Figure 1 [smr.x1.ps]). However, most SMRs are less than one, even with adjustment for occupation (Figure 2 [smr.x1.occ.ps]), suggesting healthy worker effect beyond the reach of our alignment with occupations reported in the NHIS. This may in part highlight the differences between these WTC responders and workers in general. Responders to the 9/11 disaster were unequivocally on the job, while the NHIS cohort is reporting how they work, when they are working. The assembly of an otherwise similar, *working* comparison group may help to diminish this bias.

Other chronic health conditions have been studied. In their analysis of the WTC HR cohort [n ≈ 37,000], Miller-Archie, et al (2014) reported significant association between posttraumatic stress disorder (PTSD) and new-onset diabetes, consistent with similar findings observed in other contexts. PTSD is recognized as a risk factor for diabetes, and is well-documented among WTC responders [cite]. To look for evidence of cardiovascular disease due to WTC, Jordan, et al (2013) related exposures assessed in the WTC HR cohort [n ≈ 55,000; NY residents] to hospital discharge data maintained by the state New York. They found heart and cerebrovascular disease to be significantly associated with WTC exposure through 2010, consistent with the earlier report of Brackbill, et al (2006).

The protective effect of respirator use shown in our analysis echoes the findings of Wheeler, et al (2007), where new onset asthma among rescue and recovery workers from the HP cohort [n ≈ 26,000] was associated with WTC exposures and occupations. Apart from the occupation-adjusted SMR for diabetes in women in 2002, where variability is high due to the small number of reported cases, we found the prevalence of diabetes to be lower than expected per NHIS. This may again be a manifestation of healthy worker effect. The opposition of our results to those of Miller-Archie, et al (2014) may be a consequence of endpoint definition; we used lifetime diabetes, while they reported new-onset. The significantly higher prevalence of male hypertension in the later years of follow-up may be explained by a causal pathway from WTC exposure to PTSD to elevated BMI. There is an upward trend in female hypertension in this same time frame, whether adjusting for age or occupation, which may also warrant further monitoring. While the prevalence of stroke is well below that of NHIS, this condition also exhibits an increasing trend in these nine years after 9/11.

Strengths and Limitations

One benefit of the lifetime assessment of each health condition as analyzed here is in the quality of the information obtained. We considered use of the diagnosis date, if available, to additionally inform our analysis of each health condition, and concluded that accurate, comparable dates of diagnosis from these vastly different surveys were not available.

Our findings should be interpreted in the context of several limitations. The main limitation of this study is the use of self-reported case definitions from both surveys (WTC RHC and NHIS). Among WTC exposures, we were particularly interested in the reported arrival time to the WTC site because this variable has been the only predictor of most WTC related health problems reported and has been used by other investigators as a surrogate for the amount of dust exposure [ref]. Investigating this further may require substantial effort, including verification of the paper questionnaires of historical data over 10 years.

Other potential biases discussed in the context of WTC cohorts include self-selection and recall biases. It is possible that sicker responders may have been more likely to enroll in the WTC RHC in the early period and also attend follow-up exams more frequently. The self-selection bias can be minimized if the cohort recruited close to all of the exposed population. Savitz [cite] predicted that approximately 40,000 people responded or volunteered to 9/11. If true, 36% of eligible responders may not have enrolled which may bias measurements of association in our analysis. If those not included have an inverse association from what we observed (i.e., respirator use increased asthma), our findings may be severely biased. However we believe that the likelihood of observing an inverse association would be very low, as the association we observed is well supported from previous literature.

Recall bias can be critical in this analysis because the WTC program is an open cohort and responders can enroll in the program at any time, which requires remembering events from 10 years ago or more. Remembering the type of respiratory protection used within a specific period (9/11-9/18) can be a great challenge for later enrollees. In general, less sick or healthy people are less likely to remember their exposure (unintentional recall bias). Furthermore, people may be less likely to report respirator use if there is any disadvantage associated with use of respiratory protection (intentional recall bias). However, the association between asthma and respirator use is not widely known; thus, we believe the chance of this intentional recall bias of asthma cases reporting more/less use of respirator masks would be less likely.

Ekenga, et al (2011) described the potential for selection bias in respiratory health outcomes, where symptomatic people were more likely to enroll for clinical follow-up. Some estimate of this excess likelihood would be useful. In our study, classification error in the form of recall bias or misunderstandings of participant medical histories may be substantial. Considering the reporting of obstructive airway diseases in the WTCHP Fire Department of New York (FDNY) cohort, Weakley, et al (2013) shed some light on this issue, where asthma exhibited the highest sensitivity (69%) and overall agreement (92%) between self-report and FDNY physician diagnoses [n ≈ 8,000]. In their analysis of new onset asthma among rescue and recovery workers from the HR cohort [n ≈ 26,000], Wheeler, et al (2007) cite the comparability of pre-9/11 self-reported asthma rates with NHIS and the 2002 NYC Community Health Survey (Garg, et al, 2003) as evidence against over-reporting asthma by study participants. With incentives for care systems as well as individuals to connect health outcomes to the WTC disaster, there remains concern about potential biases *post*-9/11.

CONCLUSION

We found that asthma was the main health problem among WTC responders, and identified trends in cancer, hypertension, and stroke that warrant further analysis and continued follow-up of WTC responders. We also found an apparent protective effect against asthma with respirator use. This is an important finding not only for the future disaster preparedness but also for protecting general workers from daily occupational exposure.

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Table 1. Case Definitions of Each of the Five Health Conditions in the National Health Interview Survey (NHIS) and the World Trade Center Responders Health Consortium (WTC RHC).

Condition	NHIS [1]	WTC RHC [2]
Asthma	Have you EVER been told by a doctor or other health professional that you had asthma?	Has a doctor ever diagnosed you with asthma, cough variant asthma, or reactive airways dysfunction syndrome (RADS)? ... If Yes, which: ____ Asthma ____ Cough variant asthma ____ RADS
Cancer	Have you EVER been told by a doctor or other health professional that you had ... Cancer or a malignancy of any kind?	Has a doctor ever told you that you had cancer?
Diabetes	Have you EVER been told by a doctor or other health professional that you have diabetes or sugar diabetes?	Has a doctor ever told you that you had diabetes?
Hypertension	Have you EVER been told by a doctor or other health professional that you had ... Hypertension, also called high blood pressure?	Has a doctor ever told you that you had high blood pressure?
Stroke	Have you EVER been told by a doctor or other health professional that you had ... A stroke?	Were you ever diagnosed with stroke?

[1] ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Survey_Questionnaires/NHIS/2010/English/qadult.pdf.

[2] All except stroke: WTC RHC Form *IAMQ_v1_Logician_marked*. For stroke: WTC RHC Form *IAMQ Longitudinal Variables Map*.

Table 2. Distribution of Prevalence Among Responders for Each of Five Health Conditions, and Characteristics of All Responders in the Study.

Variable	Asthma		Cancer		Diabetes		Hypertension		Stroke		Total	Total for stroke
	n	%	n	%	n	%	n	%	n	%	n	n
Lifetime Prevalence	3,914	15.2	976	3.8	1166	4.5	5780	22.4	349	2.06	25787	16975
Age at the baseline visit												
18-30	235	14.8	10	0.6	12	0.8	104	6.5	5	0.0	1593	1032
31-40	1407	15.2	139	1.5	176	1.9	1286	13.9	48	0.3	9241	6088
41-50	1583	15.9	357	3.6	443	4.5	2364	23.7	115	0.7	9962	6524
51-60	579	14.3	302	7.4	413	10.2	1574	38.8	130	0.8	4059	2690
61-older	110	11.8	168	18.0	122	13.1	452	48.5	51	0.3	932	641
Sex												
Male	3092	14.0	797	3.6	1016	4.6	5208	23.6	311	1.8	22088	14639
Female	822	22.2	179	4.8	150	4.1	572	15.5	38	0.2	3699	2336
Race												
White	2247	14.7	737	4.8	565	3.7	3409	22.3	218	1.3	15.272	10518
Black	503	17.4	79	2.7	218	7.6	877	30.4	48	0.3	2889	1871
Asian	50	13.9	8	2.2	36	10.0	96	26.7	9	0.1	360	242
Other	120	16.6	12	1.7	28	3.9	145	20.1	4	0.0	723	515
Unknown	994	15.2	140	2.1	319	4.9	1253	19.2	70	0.4	6543	3829
Ethnicity												
Hispanic	995	16.3	93	1.5	290	4.8	1100	18.1	72	0.4	6091	4018

Non-Hispanic	2145	14.9	626	4.4	602	4.2	3342	23.3	226	1.3	14.354	10180
Unknown	774	14.5	257	4.8	274	5.1	1338	25.1	51	0.3	5342	2777
Education												
Some or graduated from high school	991	12.6	272	3.5	465	5.9	1875	23.8	135	0.8	7885	5348
Two year college	1654	16.5	355	3.5	433	4.3	2278	22.7	121	0.7	10057	6605
Graduated from college or graduate school	1168	16.7	326	4.7	220	3.1	1435	20.5	82	0.5	7002	4493
Unknown	101	12.0	23	2.7	48	5.7	192	22.8	11	0.1	843	529
Income												
<$30,000	269	11.9	55	2.4	100	4.4	443	19.5	32	0.2	2270	1554
$30-60,000	958	16.1	229	3.9	340	5.7	1396	23.5	81	0.5	5952	3872
$60-80,000	941	15.9	244	4.1	243	4.1	1297	21.9	88	0.5	5921	3849
>$80,000	1072	16.2	303	4.6	260	3.9	1544	23.4	62	0.4	6606	4395
Unknown	674	13.4	145	2.9	223	4.4	1100	21.8	86	0.5	5038	3305
Marital status												
Single	653	16.6	102	2.6	124	3.2	653	16.6	55	0.3	3926	2530
Married or partnered	2552	14.6	697	4.0	812	4.6	4085	23.3	220	1.3	17531	11681
Separated or divorced	587	16.6	137	3.9	167	4.7	830	23.4	63	0.4	3543	2391
Widowed	52	17.7	28	9.5	26	8.8	105	35.7	11	0.1	294	196
Unknown	70	14.2	12	2.4	37	7.5	107	21.7	0	0.0	493	177
Cigarette smoking												
Never	2424	16.0	515	3.4	589	3.9	3271	21.6	166	1.0	15134	9818
Current smoker	476	12.4	99	2.6	155	4.0	728	19.0	57	0.3	3833	2479
Former smoke	950	15.8	344	5.7	390	6.5	1666	27.7	113	0.7	6011	4048
Unknown	64	7.9	18	2.2	32	4.0	115	14.2	13	0.1	809	530
Pre-9/11 occupation												

Protective service	1816	17.2	393	3.7	370	3.5	2244	21.2	87	0.5	10590	6525
Construction	389	11.6	111	3.3	175	5.2	743	22.2	58	0.3	3350	2321
Utility	229	15.8	54	3.7	111	7.7	417	28.8	30	0.2	1447	1003
Transportation	111	13.1	33	3.9	67	7.9	242	28.5	19	0.1	849	560
Business	142	16.3	58	6.7	42	4.8	215	24.7	15	0.1	870	592
Other	578	12.6	182	4.0	224	4.9	1020	22.3	98	0.6	4571	3158
Unknown	649	31.6	145	6.8	177	8.7	899	23.0	42	0.2	4110	2816
Arrival to WTC site												
On 9/11 in the dust cloud	877	17.9	205	4.2	225	4.6	1179	24.0	70	0.4	4911	3273
On 9/11 not in the dust cloud	952	16.2	219	3.7	263	4.5	1345	22.8	68	0.4	5889	3772
9/12-9/14	1157	14.8	301	3.9	328	4.2	1660	21.3	96	0.6	7795	4976
9/15-9/30	637	12.7	178	3.6	237	4.7	1086	21.7	74	0.4	5006	3320
On or after October/unknown	196	12.7	73	6.6	113	10.1	362	23.4	41	0.2	2186	1634
Hours of work in Sept												
Median (Interquatile range)	144	55-228	112	37-210	120	46-216	132	50-225	144	56-228	144 (565-228)**	145 (60-228)**
Type of respiratory protection used in 9/11-9/18												
Didn't wear one	756	17.3	198	4.5	226	5.2	1003	23.0	46	0.3	4371	2711
Dust/ surgical/ disposable mask	1958	16.7	474	4.0	533	4.5	2716	23.1	170	1.0	11739	7503
Half/full-face respirator	517	11.4	125	2.8	175	3.9	937	20.6	61	0.4	4547	3305
Unknown/Not in the period (9/11-9/18)	683	26.8	179	7.0	232	8.9	1124	43.8	72	0.4	5130	3456
Location of work in September 2001												
On the pile/in the pit	1407	15.9	321	3.6	360	4.1	1883	21.3	118	0.7	8860	5840
Adjacent to pile/pit	1741	14.6	439	3.7	529	4.5	2691	22.6	151	0.9	11901	7854
Landfill	114	16.6	31	4.5	34	5.0	149	21.7	11	0.1	687	447

Barges/Loading piers	43	16.9	14	5.5	15	5.9	68	26.7	8	0.0	255	175
Elsewhere	311	37.9	14	4.1	14	4.1	90	26.5	12	0.1	340	222
Unknown	298	13.3	157	8.7	214	11.5	899	48.4	49	0.3	3744	2437

* History of stroke diagnosis was collected from follow-up visit, not from the baseline visit. Therefore total N for stroke is the total number of participants at the second visit.

** Median (interquatile range) instead of total N

Table 3. Adjusted[1] Incidence Rate Ratios (IRRs) for Asthma, Obtained by Internal Comparison of WTC Exposures.

WTC Exposure	IRR	95% CI	
Pre-9/11 occupation			
Construction	1		
Protective service	1.31	1.12	1.54
Utility	1.39	1.11	1.73
Transportation	1.24	0.94	1.63
Business	1.29	0.99	1.66
Other	1.21	1.01	1.44
Arrival at WTC site			
On 9/11 in the dust cloud	1		
On 9/11, but not in the dust cloud	0.81	0.71	0.93
On September 12–13	0.85	0.74	0.97
On September 14–30	0.80	0.68	0.95
On or after October 1, 2001	0.91	0.58	1.43
Type of respiratory protection used in 9/11-9/18			
Did not wear respiratory protection	1		
Dust/ surgical/ disposable mask	0.89	0.78	1.00
Half/full-face respirator	0.70	0.60	0.82
Other/don't know/missing	0.80	0.66	0.98
Not in the period (September 11–18)	0.82	0.64	1.07
Location of work in September 2001			
On the pile/in the pit	1		
Adjacent to pile/pit	1.18	0.97	1.43
Landfill	0.98	0.81	1.18
Barges/Loading piers	0.91	0.64	1.30
Elsewhere	0.99	0.60	1.63
Don't know/missing/after September 2001	1.12	0.78	1.60

[1] IRRs adjusted for age group, gender, race, ethnicity, education, income, marital status, and cigarette smoking.

Table 4. Participation Rates by Visit.

Last Visit	Number Completed Through Visit	%	Cumulative Percent
Baseline	9,600	37.2	37.2
Follow-Up 1	6,512	25.3	62.5
Follow-Up 2	4,836	18.8	81.2
Follow-Up 3	3,007	11.7	92.9
Follow-Up 4	1,740	6.8	99.6
Follow-Up 5	92	0.4	100.0
Total	25,787	100.0	

Appendix 3

World Trade Center Disaster Exposure-Related Probably Posttraumatic Stress Disorder among Responders and Civilians: A Meta-Analysis

PLOS ONE

World Trade Center Disaster Exposure-Related Probable Posttraumatic Stress Disorder among Responders and Civilians: A Meta-Analysis

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Abstract

The World Trade Center (WTC) disaster on September 11, 2001 was an unprecedented traumatic event with long-lasting health consequences among the affected populations in the New York metropolitan area. This meta-analysis aimed to estimate the risk of probable posttraumatic stress disorder (PTSD) associated with specific types of WTC exposures. Meta-analytical findings from 10 studies of 3,271 to 20,294 participants yielded 37 relevant associations. The pooled summary odds ratio (OR) was 2.05 (95% confidence interval (CI): 1.82, 2.32), with substantial heterogeneity linked to exposure classification, cohort type, data source, PTSD assessment instrument/criteria, and lapse time since 9/11. In general, responders (e.g. police, firefighters, rescue/recovery workers and volunteers) had a lower probable PTSD risk (OR = 1.61; 95% CI: 1.39, 1.87) compared to civilians (e.g. residents, office workers, and passersby; OR = 2.71, 95% CI: 2.35, 3.12). The differences in ORs between responders and civilians were larger for physical compared to psychosocial exposure types. We also found that injury, lost someone, and witnessed horror were the three (out of six) most pernicious exposures. These findings suggest that these three exposures should be a particular focus in psychological evaluation and treatment programs in WTC intervention and future emergency preparedness efforts.

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Introduction

The World Trade Center (WTC) disaster on September 11, 2001 (9/11) was an unprecedented traumatic event to the responders and civilians in the New York metropolitan area and beyond. In the wake of the disaster, many programs were established to provide physical and mental health screening, monitoring and/or treatment service to affected individuals. Three major programs established in the New York metropolitan area are: the Fire Department of the City of New York Medical Monitoring Program (the FDNY), the WTC Health Registry (the Registry), and the WTC Health Program (WTC-HP, formally known as the WTC Medical Monitoring and Treatment Program or MMTP). The FDNY program was implemented in 2001 to screen and monitor FDNY members involved in the rescue and recovery efforts of 9/11. This group consists predominantly of active firefighters, but also emergency medical service workers, FDNY administrative personnel, and some retired FDNY as well. The Registry was established in July 2002 by the New York City Department of Health and Mental Hygiene in collaboration with the Agency for Toxic Substances and Disease Registry. Registry enrollees include rescue/recovery workers and volunteers (i.e. non-traditional responders), passersby, and school children and staff, residents and office workers in lower Manhattan. The WTC-HP is a Center for Disease Control and Preventions (CDC) funded consortium of 5 centers including the Department of Community and Preventive Medicine at the Mount Sinai School of Medicine, the Bellevue/New York University Occupational and Environmental Medicine Clinic, the State University of New York-Stony Brook, the Center for the Biology of Natural Systems at Queens College, and the Clinical Center of the Environmental & Occupational Health Sciences Institute at the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School in New Jersey. Founded in July 2002, the program monitors and treats police and non-traditional responders (e.g. recovery/rescue workers and volunteers, construction workers, transportation workers, etc.) who participated in the rescue/clean-up/recovery work from 9/11/2001 until 12/31/2001.

During more than a decade after the 9/11 event, a number of studies from the three centers [1–13] and from other WTC research programs [14,15] investigated a range of physical and mental health conditions among both responders and civilians. Among the mental health conditions, probable posttraumatic stress disorder (PTSD), measured with check-lists tailored to the event, stands out as one of the major syndromes that appears to have endured over the decade following the disaster [16,17]. Recent reviews [17–21] also point to specific risk factors that were found to be associated with probable PTSD in these samples, including sociodemographic and occupational characteristics, types of exposure, social support, and medical comorbidity. The focus of this study is to extend the scope of these reviews by providing a quantitative effect size estimate of PTSD risks attributable to specific WTC exposures, while taking into account the discrepancies in study designs.

By studying research results accumulated more than a decade since the event, we aim to understand the psychological health impact of 9/11 in an effort to provide insights that could enhance current intervention and future disaster preparedness programs. To this end, we conducted a meta-analysis to quantify the odds ratio (OR) for probable PTSD associated with specific WTC exposures, and to examine whether discrepancies in aspects of study design such as WTC exposure classification and cohort type (i.e. responders vs. civilians) affected PTSD risk.

Methods

Data source and searches

Relevant studies were identified by searching PubMed databases for all published articles up to 22 April 2013, using the relevant search terms such as "world trade center", "WTC", "world trade center disaster", "WTCD", "September 11", "9/11", "posttraumatic stress disorder", "PTSD", "post traumatic stress disorder", "world trade center medical monitoring and treatment program", "WTC-MMTP", "Medical Monitoring and Treatment Program", "MMTP", "world trade center health registry", "WTC-HR", "WTCHR", "Health Registry", "HR", "New York City Department of Health and Mental Hygiene", "NYC DOHMH", "NYC", "DOHMH", "Fire Department of the City of New York", "FDNY", "medical monitoring program", "MMP", "FDNY-WTC-MMP", "WTC-MMP", and "FDNY-MMP".

Inclusion/Exclusion criteria

We selected studies for the meta-analysis based on the following criteria: 1) published in an English-language journal; 2) peer-reviewed; 3) original research papers; 4) focused on adult populations; 5) conducted in the New York metropolitan area; 6) specified the PTSD measurement instrument and criteria used; 7) specified exposure levels; 8) listed specific numbers of study participants who were classified with and without PTSD corresponding to the exposure levels.

Data extraction

Data relevant to the associations between WTC exposure and PTSD risks were extracted. Eligible articles and extracted data were examined by three investigators (B.L., L.H.T., and H.K.). Data extracted included cohort types (e.g. firefighters, police, non-traditional responders, residents, office workers, and passersby), data source (i.e. FDNY, Registry, WTC Health Program, and others), exposure types, PTSD assessment instrument/criteria, sample size, probable PTSD prevalence, the number of subjects with and without probable PTSD (P+/P-) among those with high vs low or no WTC exposure.

Statistical analysis

We used the DerSimonina-Laird (DL) random-effects model [22] to calculate the summary effect size of OR and the 95% confidence interval (CI) (i.e. OR [95% CI]). Analysis was conducted using R software with the *metfor* Package [23]. Variability across individual ORs was assessed by five variables: the between-study variance (τ^2); the standard error (SE) of the overall population effect size estimate; the Cochran's Q-test (p-value reported here); I^2 value; and H^2 statistics [24]. For each study, we approximated an average lapse time based on the differences between 9/11 and the earliest and latest enrollment time (e.g. if a study enrollment period was 2001–2005, the average lapse time was (0+4)/2 = 2 years). We explored the influence of four potential moderators, namely, cohort type, WTC program, PTSD measure, and lapse time. To do this, we used mixed-effects models and included one moderator in the model at a time.

Sensitivity analysis was conducted to assess potential substantial changes in the summary effect size by a few individual data points. This was done by using the *influence()* function, which provides visual examination, and by the *leav1out()* function, which is conducted by repeatedly fitting the DL model (without moderators) while leaving out one study at a time. We also visually examined the symmetry in the funnel plot for publication bias. In addition, asymmetry of the funnel plot was assessed using the rank correlation analysis (i.e. the Begg's method, [25]) and linear regression analysis (i.e. the Egger's method,[26]). Both the Begg's and Egger's tests were used to examine if there were significant correlations between the effect estimates and their variances.

Results

Systematic search results

Of the 95 English-language articles resulting from the search, 54 studies were excluded after reviewing the abstracts in the first round of screening (Figure. 1) due to at least one of the following reasons: case report (n = 4), comment/editorial/opinion piece (n = 4), review paper (n = 6), youth population (n = 7), not PTSD related (n = 24), not restricted to the New York metropolitan area (n = 4), and not WTC related (n = 5). An additional 31 studies were excluded after reviewing the full-text due to at least one of the following reasons: PTSD criteria not specified (n = 3), papers focused on validating a modified PTSD questionnaire (n = 2), lack of specific numbers of study participants who were classified with and without PTSD that corresponded to the exposure levels presented in the paper (n = 25), and significant sample overlap with another paper included in the analysis (n = 1). Our search strategy and inclusion/exclusion criteria resulted in a total of 10 articles for the current meta-analysis ([1–7,9,12,13]; Table 1). Four papers (b–d, and f) were from the Registry, three studies (a, h, and j) were from the FDNY, and three from the WTC-HP (e, g, and i).

Sample Characteristics

The 10 articles we identified had cohorts that ranged from N = 3,271 to N = 20,294 (Table 1). Among them, five studies (a, e, g, h, i, and j) focused solely on responders, three papers (c, d, and f) focused solely on civilians, and one article (b) included a mix of responders and civilians. The participants were enrolled at different time relative to 9/11 ranging from a few months to 9 years, with an estimated average lapse time of 3.5 years. The responders were predominantly male (>85%) and white, ranging from 49–64% of police and up to 94% of firefighters. The male-to-female ratios were more balanced among civilians, and 62–71% of them were white.

Overall the pooled samples included three cohorts from the three major WTC program centers that captured the diverse populations affected by the WTC disaster in the New York Metropolitan area. The overlaps in participants among the three programs ranged from less than 1% between the WTC-HP and FDNY to approximately 20% for responders between the Registry and WTC-HP [27]. The total number of FDNY participants ranged from 1159 to 8869 for each of the nine survey cycles between 2001 and 2010 [6]. One longitudinal study of FDNY

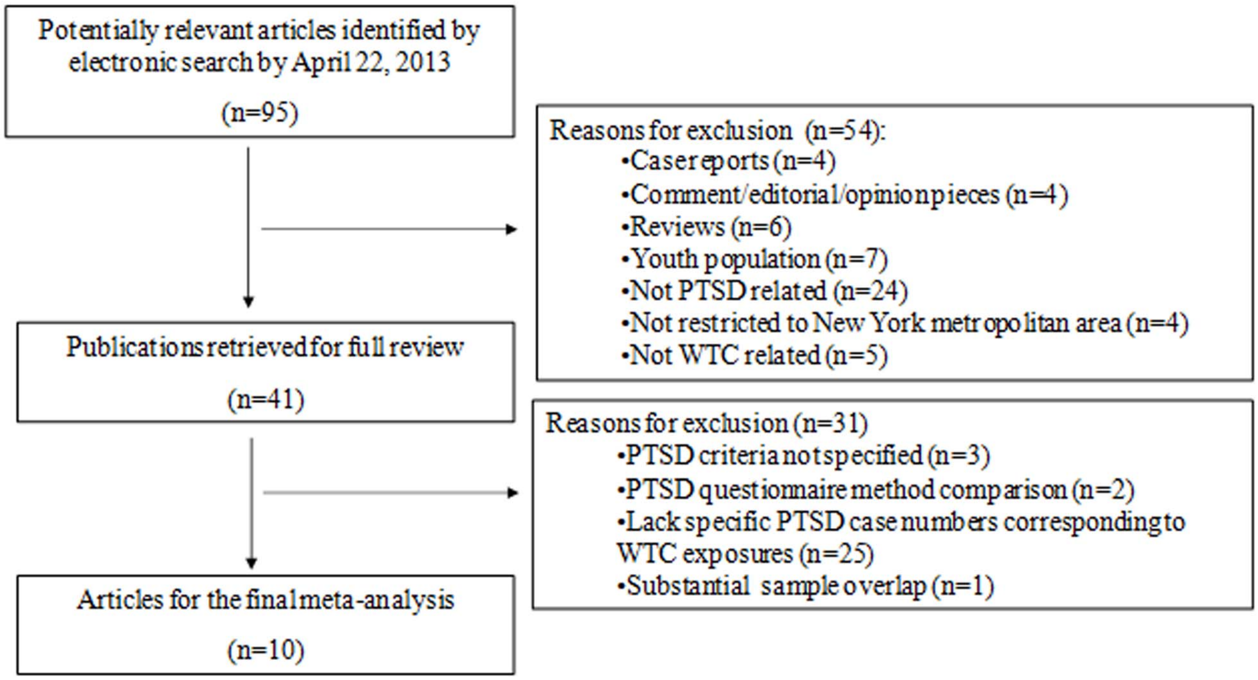

Figure 1. Flow chart of study selection.
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([28]; not included in this meta-analysis) reported an approximately 83% of the baseline enrollees participated in the 3–4 years follow-up. For the Registry, approximately 68% of the participants from the Wave 1 enrollment (2003-2004) also participated in Wave 2 (2006–2007) [2]. Within the WTC HP during the period of 2002–2012, the average number of participation of follow-up examinations was 1.1.

To minimize the shared sample problem while capture the maximum overall sample size, cohort types, and exposure categories for the meta-analysis, we carefully selected these 10 studies. The final extracted data used for the meta-analysis were presented in Table S1 as supplement information. In general, individual data with the largest number of participants were used during the analysis. For example, for civilian residents with exposure of "witnessed horror" and "injury", data from DiGrande et al (n = 11037; [4]) were used instead of those from the study by Brackbill et al. (n = 5852; [2]). Further, analysis was conducted on a subset of data (Table S1) with minimal shared samples within the same exposure type.

Assessment of WTC exposure

A total of six types of WTC exposures was summarized from the 10 studies with original and derived exposure types presented in Table 2. Overall, these exposures were coarsely grouped into two major categories: those that focused on physical exposure (i.e. arrival time, dust cloud, injury, and work duration) and those focused on psychosocial aspects (i.e. lost someone and witnessed horror). While there were more exposure types listed in the original articles (32 distinct exposure types; data not shown), many of them were unique to a single study, and thus were not applicable to the goals of the meta-analysis. That is, each of the 6 exposure types in this review (Table 2) had at least two individual OR estimates.

It is also worth noting that large variations existed with regard to how WTC exposures were classified among the original studies (Table 2). For instance, studies from the FDNY (a, h, and j) and Registry (b) both used a 4-level exposure variable to define "arrival time", while a 2-level "arrival time" was used in the two WTC-HP studies (g and i). Furthermore, large differences were also found in the specific cut-off points and the overall time durations covered in these studies (Table 2). To reconcile the discrepancies in the original exposure characterizations, we derived a dichotomized variable for each exposure using the lower or no exposure as the reference group in calculating probable PTSD risks (Table 2, e.g. late arrival, short work duration, and absent of exposure). Among these exposure types, "arrival time" and "work duration" were unique to responders, while others ("dust cloud", "injury", "lost someone", and "witnessed horror") were shared by both responders and civilians.

Assessment of PTSD

Because all these PTSD assessments were based on self-report and not clinical diagnostics, the PTSD referred to in this study is probable PTSD. All but one [1] of the studies included in this meta-analysis administered the 17-item PTSD Checklist-Civilian (PCL) with the WTC as the focal event. The PCL assesses PTSD symptom severity for the last 30 days on a scale of 1 = not at all to 5 = extremely. Probable PTSD was determined using a cut-off point for the total severity score, or by severity scores congruent with the symptom criteria of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV,[30]), namely, at least 1 B item (question 1–5, for intrusion symptoms rated moderate-severe), plus 3 C items (questions 6–12, for avoidance/numbing symptoms), and plus 2 D items (questions 13–17, for hyperarousal symptoms). The one exception was a FDNY study [1] in which a modified PCL was administered, which has been validated for use in firefighters and detailed elsewhere [1,6,29]. Briefly, 14 of the 17 standard PCL symptoms were included in the modified version, the answers were rated on a binary scale (i.e. did or did not experience each symptom), and a cutoff of ≥9 (out of 14) was

Table 1. Descriptions of the ten WTC studies included in the meta-analysis.

ID	Articles	Cohort Types	WTC Programs	Enrollment period	PTSD assessment (instrument/ criteria)	PTSD (%)	Total (n)	Sample Characteristics [d]
a	Berninger et al., 2010	firefighters	FDNY	2001–2005	Modified PCL [a]	14.4	10074	Male (100); Age (39.6±7.5); White (93.8)
b	Brackbill et al., 2009	non-traditional responders	Registry	2003–2004	PCL (≥44)	22.9	20294	Male (62);
		residents		&		21.3	5852	Age (25–44);
		office workers		2006–2007		25.2	14718	White (70.8)
		passersby				29.2	2087	
c	DiGrande et al., 2008	residents	Registry	2003–2004	PCL (≥44 & DMS-IV)	12.6	11037	Male (44.6); Age (46);White (62.1)
d	DiGrande et al., 2011	office workers	Registry	2003–2004	PCL (≥50)	15	3271	Male (58.8); Age (40.8±10.9); White (68.2)
e	Luft et al., 2012	Police	WTC Health Program	2002–2008	PCL (≥50)	5.9	8508	Male (85); Age (40.8±6.6)
		non-traditional responders				23	12333	Male (86.1); Age (44.4±9.9)
f	Nair et al., 2012	residents	Registry	2003–2004	PCL(≥44 &DSM-IV)	8.5[b1]	16363	Male (48.3); Age (18–65+)
				& 2006–2007		5.8[b2]	16363	Male (48.3);White (67.3); Age (25–44)
g	Pietrzak et al., 2012	police	WTC Health Program	2002–2008	PCL (≥50 & DSM-IV)	5.4[c]	8466	Male (85.3); Age (35–59); White (48.9)
h	Soo et al., 2011	firefighters	FDNY	2006–2007[d]	PCL (≥44 & DSM-IV)	7.7	4343	Male (100); Age (38.9±7.9); White (93.7)
i	Stellman et al., 2008	police	WTC Health Program	2002–2006	PCL (≥50)	11.1	10132	Male (87.3); Age (median:40); White (64)
j	Webber et al., 2011	Firefighters & EMS workers	FDNY	2007–2010	PCL (≥44 & DSM-IV)	6.9	10867	Male(89.2); Age (25–44); White (89.2)

Note: PTSD (%) = probable PTSD prevalence. n = total numbers of participants. FDNY = Fire Department of the City of New York. PCL = PTSD Checklist-Civilian Version, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th edition. [a], PTSD assessed by a modified PCL. [b1], those with PTSD alone; [b2], those with both PTSD and lower respiratory symptoms. [c], full PTSD. [d], the percentages (%) of male sex and white ethnic/race, and age in years (age ± standard deviation, median, or age bracket with the largest percentage) were shown in (). [d], results from 2006–2007 was used in this meta-analysis.
doi:10.1371/journal.pone.0101491.t001

Table 2. Summary of the six WTC exposure types from the ten studies included in the meta-analysis.

Exposure types		Studies	Exposure classifications	
(used in the Meta-Analysis)			Summarized	Original
physical	Arrival Time	a , h, j	9/11-9/12	level 1: am on 9/11;
exposure	(Early vs		(sum of levels 1–3)	level 2: pm on 9/11;
	Otherwise*)		vs level 4*	level 3: day 2;
				level 4: day 3–14 *
		b	9/11	level 1: 9/11 (on pile);
			(sum of levels 1–2)	level 2: 9/11 (other WTC site);
			vs	level 3: 9/12-9/17 (any WTC site);
			otherwise (sum of levels 3–4)	level 4: 9/18/2001-6/2002, any WTC site *
		g	9/11 or 9/12	vs otherwise *
		i	Present 9/11-9/12:	Yes vs No*
	Dust Cloud	b, f	Yes (sum of levels 1–2) vs None*	level 1: intense; level 2: some; level 3: none*
	(Yes vs No*)	c, d	Caught in dust cloud:	Yes vs No*
		e	Worked in dust cloud:	Yes vs No*
	Injury	b	Sustained injury on 9/11:	Yes vs No*
	(Yes vs No*)	d	Injured on 9/11:	Yes vs No*
	Work Duration	b	>3 months	Days worked in any WTC site: level 1:1-7;
	(Long		vs otherwise (sum of levels 1–3) *	level 2: 8–30;level 3: 31–90;level 4: >90
	vs	e	≥ the top quartile (1353 hours	or 1.89 months) vs otherwise *
	Otherwise*)	g	≥ the median (total hours worked	608 hours or 0.84 months) vs otherwise *
		i	>5.5 months (level 5)	Time at site: level 1: ≤2 weeks;
			vs	level 2: up to 1.5 months;
			otherwise (sum of levels 1–4)*	level 3: up to 3 months;
				level 4: up to 5.5 months;
				level 5: >5.5 months
psychosocial	Lost Someone	b	Lost someone (sum of levels 1–4)	Loss/death of other on 9/11:
exposure	(Yes vs No*)		vs	level 1: Spouse; level 2: Other family member;
			None *	level 3: Coworker; level 4: Acquaintance;
				level 5 : None*
		g	Lost someone on 9/11:	Yes vs No*
	Witnessed Horror	b	Witnessed traumatic or	horrific event on 9/11: Yes vs No*
	(Yes vs No*)	c	Witnessed horror on 9/11:	Yes vs No*
		g	Exposed to human remains:	Yes vs No*

Note: Dichotomized exposure indicators were derived from exposure classifications used in the original studies. * indicates the reference group. Details of studies (a–j) were shown in Table 1.

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determined to be equivalent to a cutoff score of 44 in conjunction with the DSM-IV symptom criteria. As shown in Table 1, among the 10 studies, probable PTSD was operationalized by a cut-off score of 44 or 50 with or without the presence of DSM-IV criterion symptoms, and the PTSD prevalence ranged from 5.4% to 29.2% (Table 1).

Effect size analysis

Based on the exposure classification, a total of 37 ORs (each OR was assigned to a unique internal identification in the analysis, Table S1) were available from the 10 studies for the final meta-analysis. We first calculated the overall summary of PTSD risk regardless of the specific WTC exposure type. The result showed that the overall PTSD risk was 2.05 [1.82, 2.32] with substantial heterogeneity (p-value <0.001 for the Cochran Q test). The I^2 statistics (0.97 [0.96, 0.98]) was close to 100% and $H^2>5$ (i.e. 31 [23, 59]). The between-study variance (τ^2) was 0.14 (SE = 0.04). The heterogeneity was partly due to the influence of potential moderators (p-value <0.01, mixed-effects models), such as cohort type, WTC program, PTSD measure, and lapse time since 9/11, respectively. Most notably, responders had a significantly lower estimated OR than civilians ($p<0.001$), and the Registry had a higher OR than the FDNY ($p<0.01$).

We found little evidence of publication bias from visually examining the symmetry of the funnel plot (Figure 2), which was also confirmed by both the Begg's test (p-value = 0.89) and Egger's test (p-value = 0.93). The sensitivity analysis showed no substantial changes in the estimated summary ORs, which ranged from 2.0 [1.78–2.25] to 2.11 [1.89–2.37] with the values of τ^2 ranging from 0.11 to 0.12.

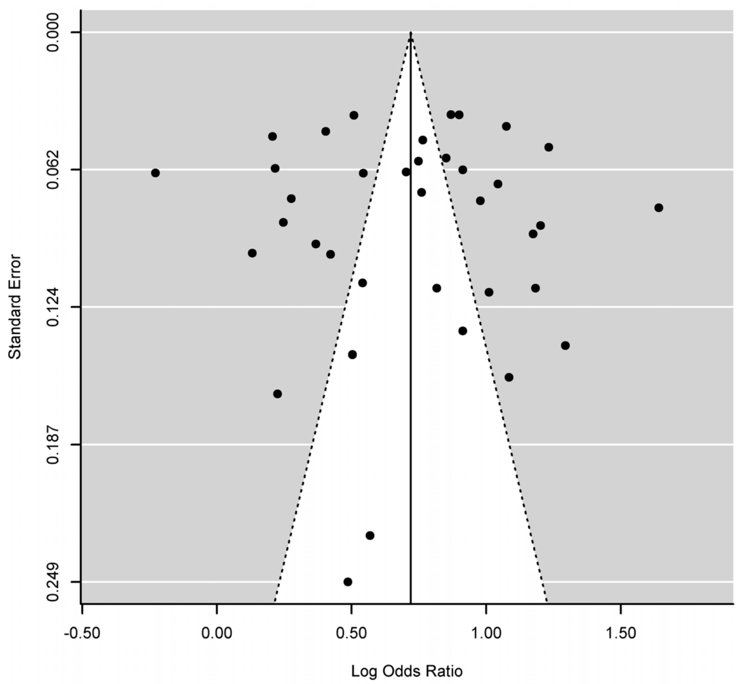

Figure 2. Funnel plot of the log odds ratios (ORs) of probable PTSD risks associated with WTC-related exposure for the meta-analysis of the ten studies included in the meta-analysis. Note: The points correspond to the 37 individual ORs. The funnel shape indicates the expected 95% confidence intervals around the summary estimate (vertical line). Little evidence of publication bias was found based on the symmetry of the funnel plot, which was also confirmed by both the Begg's test (p-value = 0.89) and Egger's test (p-value = 0.93).
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We next summarized the ORs with respect to the exposure sub-groupings that were common to both responders and civilians (Figure 3), and also stratified by responders (Figure 4) and civilians (Figure 5), respectively. When both responder and civilian data were combined based on the four common exposure types (Figure 3), the overall summary OR was 2.47 [2.20, 2.76] (n = 24), with the highest OR found for exposure to "injury" (3.69 [2.91, 4.68]), and the lowest for "dust cloud" exposure (2.15 [1.81, 2.56]). The mixed-effects model showed significant influence ($p < 0.05$) of cohort type (responders < civilians, $p < 0.001$), WTC program (WTC-HP < Registry, $p < 0.001$), and PTSD measure (PCL cutoff score of 50<44, $p < 0.001$), but not from lapse time ($p = 0.14$).

For responders (Figure 4), the individual ORs associated with psychosocial exposure types ranged from 1.72 to 2.49 and all of the 95% CIs were above one, while ORs associated with physical exposure types ranged from 0.80 to 2.96 and some 95% CIs contained one. The summary OR among police and firefighters was 1.53 [1.25, 1.88] (n = 13), lower than that found among the non-traditional responders (1.88 [1.50, 2.34], n = 8). Among civilians (Figures 5), all the individual ORs, regardless of physical or psychosocial exposure types, were statistically significant. The highest summary ORs for civilians were seen in the "injury" exposure category (4.02 [3.01, 5.37]) followed by "witnessed horror" (2.73 [2.16, 3.46]). The ORs for "dust cloud" (2.41 [2.07, 2.80]) and "lost someone" (2.45 [1.89, 3.19]) exposures were similar. When the overall summary ORs were compared by cohort types, stronger associations were found for civilians (2.71 [2.35, 3.12], n = 16) compared to responders (1.66 [1.42, 1.94], n = 21).

Results from the additional analysis on a subset that consisted of 25 ORs (Table S1) showed similar associations seen in the full data set. WTC exposure were significantly associated with probable PTSD with an overall OR of 2.17 [1.88, 2.51] and ranging from 2.56 [2.30, 2.84] for both responders and civilians combined (Figure S1), 1.67 [1.37, 2.03] among the responders (Figure S2), and to 2.78 [2.36, 3.28] among the civilians (Figure S3).

Discussion

This meta-analysis used pooled data from WTC-related studies to evaluate and compare the probable PTSD risk associated with specific exposures among adults in the greater New York area. We found that the overall summary OR, the summary ORs by cohort types, and summary ORs for specific types of exposures from the ten studies reviewed herein were all statistically significant. This analysis confirms results from the existing body of evidence showing strong associations between a variety of WTC exposures and risk of probable PTSD for both responders and civilians.

There are several challenges to be considered in the research on associations between the WTC exposure and PTSD. Both variations in the nature of the exposure (e.g. specific type, duration, and severity of trauma exposure) and in the status of the affected individuals (e.g. age when exposure occurred, sex, education, occupation, psychiatric and physical comorbidity, coping mechanisms and capability, etc.) may influence the PTSD outcome [5,7,9,11,13,31]. In terms of characterizing the WTC exposure, given the magnitude of the impact of 9/11 and the diverse population affected by the event, it is not surprising that we found diverse exposure types across the relevant studies. However, only a handful of specific exposure types overlapped among these studies. It is also worth noting that there were large variations among the original exposure classifications in terms of exposure severity and specificity. In general, the exposure classifications were more consistent in the responder research, particularly within individual health programs, than civilian studies. For example, "arrival time" and "work duration" were ascertained in research

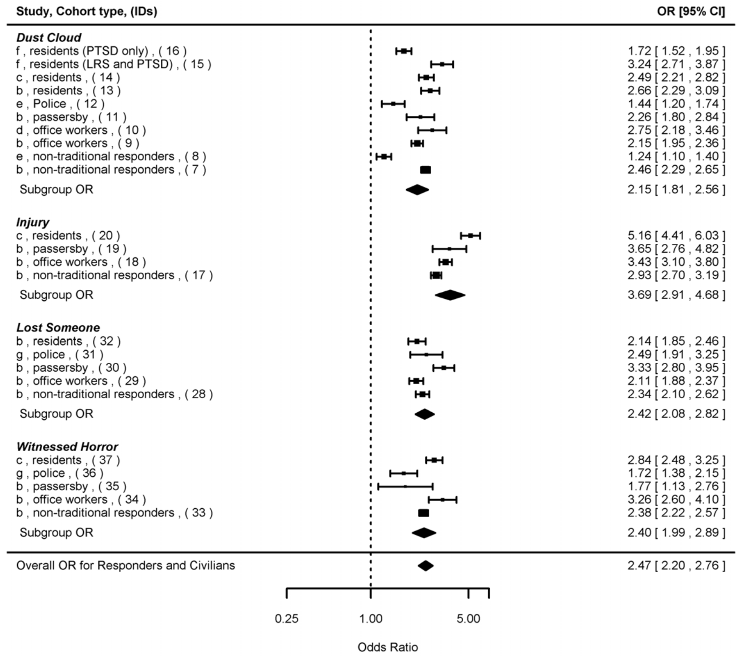

Figure 3. Forest plot of odds ratios (ORs and 95% confidence intervals) of probable PTSD risks associated with four specific WTC exposure types common between the responders and civilians. Note: Individual ORs from the original studies, summary ORs for the exposure subgroups, and the overall OR were presented. Details of the studies (a–j) and cohort types were shown in Table 1. IDs (1–37) corresponded to individual ORs in Table S1.
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on police, firefighters, and non-traditional responders, though different cutoffs were used in determining duration of the exposure among the three responder types. As a result, the severity of the WTC exposure and the consequent PTSD health outcome also varied. These discrepancies undoubtedly contributed to the large heterogeneity seen among the ORs.

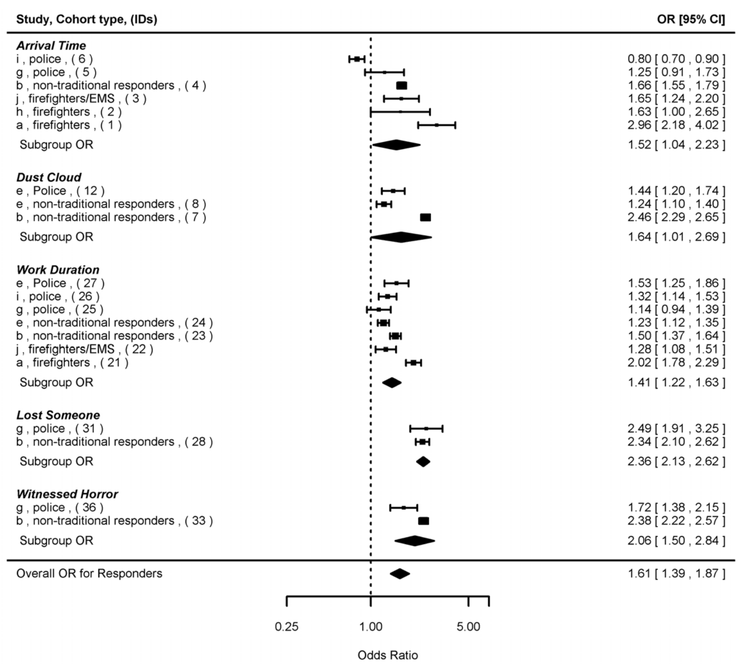

Figure 4. Forest plot of odds ratios (ORs and 95% confidence intervals) of probable PTSD risks associated with five specific WTC exposure types common among the responders. Note: Individual ORs from the original studies, summary ORs for the exposure subgroups, and the overall OR were presented. Details of the studies (a–j) and cohort types were shown in Table 1. IDs (1–37) corresponded to individual ORs in Table S1.
doi:10.1371/journal.pone.0101491.g004

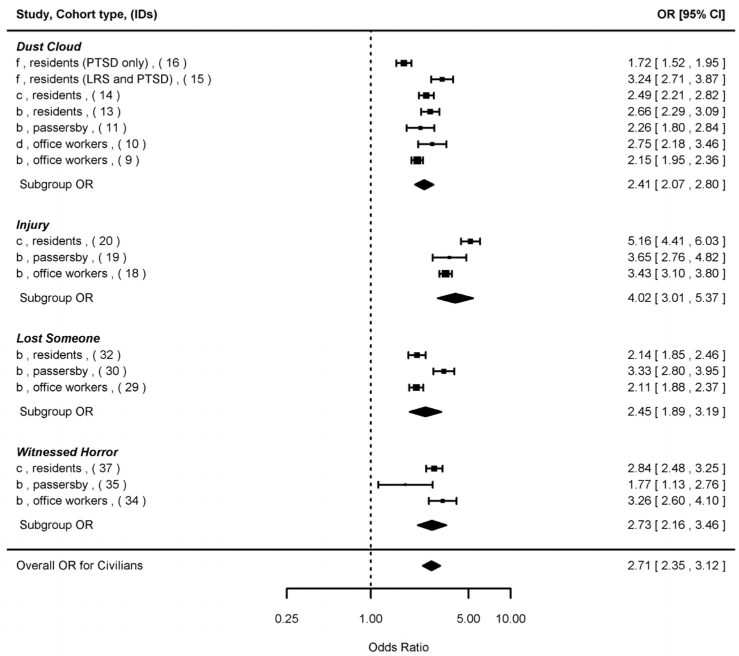

Figure 5. Forest plot of odds ratios (ORs and 95% confidence intervals) of probable PTSD risks associated with four specific WTC exposure types common among the civilians. Note: Individual ORs from the original studies, summary ORs for the exposure subgroups, and the overall OR were presented. Details of the studies (a–j) and cohort types were shown in Table 1. IDs (1–37) corresponded to individual ORs in Table S1.
doi:10.1371/journal.pone.0101491.g005

In general, the associations between exposure and probable PTSD were weaker in responders than civilians, and this difference was more pronounced for physical compared to psychosocial exposure types. On one hand, the responders faced unprecedented, treacherous working conditions at the site and were potentially under more intense physical and psychological stress. Thus, one could hypothesize that the risk of having PTSD might be higher in responders than civilian populations. On the other hand, the police and firefighters were professionally trained to work under dangerous situations, and thus had greater experience coping with disasters than civilians. Indeed, we found an overall weaker exposure-PTSD association among police and firefighters compared to the non-traditional responders (OR of 1.53 vs. 1.88), consistent with results from other studies showing traditional responders with training had lower rates of probable PTSD than non-traditional responders without prior training [32]. In this study, the benefit of training and experience was certainly reflected in the lower OR ranges seen for the physical exposure types (“dust cloud” and “injury”) among the responders (1.24–2.46 and 2.93, respectively) compared to the civilians (1.72–3.24 and 3.43–5.16, respectively). It was also reflected in the overall low and non-significant ORs in the work-related exposure among responders, with ORs ranging from 0.80 to 2.96 and from 1.14 to 2.02 for the “arrival time” and “work duration”, respectively. However, it is likely that these two physical exposure types were less sensitive in predicting PTSD compared to exposures with direct link to mental stress. Indeed, when psychosocial exposure types were considered, limited differences in ORs were found between responders and civilians. For the “lost someone” and “witnessed horror” exposure types, the associations ranged from ORs of 2.34–2.49 and 1.72–2.38 among responders, respectively, to 2.11–3.33 and 1.77–3.26, respectively, among civilians. Police and firefighters reporting these losses often sustained multiple losses of close colleagues, with entire work units massively affected. Thus, future studies of loss need to distinguish between the nature and number of losses sustained during this horrendous event.

Apart from heterogeneity in the classification of WTC exposure, other factors could also influence the relatively weaker overall exposure-PTSD associations found in responders compared to civilians. In this study, a dominant proportion of traditional responders and a majority of the non-traditional responders were males and whites, while the sociodemographic profiles of the civilian groups were more diverse. Studies have shown a general elevated prevalence in PTSD and other anxiety and mood symptoms among females compared to males and/or among Hispanic ethnicity [2,4,17,31,33,34]. Other studies have argued that concerns of repercussions could also lead to underreporting of mental health symptoms among police [35].

This paper sheds new light on the associations of WTC exposure to probable PTSD by providing quantitative estimates of the associations as indicated by ORs from the existing 9/11-related research accumulated over more than a decade. We identified three exposure types (i.e. injury, loss of life, and witnessed horror) out of six to be associated with greater PTSD risks, suggesting they should be included in emergency preparation, evaluation, and treatment programs of future disasters for both responders and civilians. Our results also showed differences in the PTSD risks were attributable to diverse exposure classifications and cohort types, as well as other moderator such as data sources, PTSD assessment instrument/criteria, and lapse time since 9/11.

Our results must also be considered in relation to study limitations. First, our meta-analysis was constrained by the availability of only 10 studies that met our selection criteria. While the summary effect size was based on 15-37 individual ORs, we also had a few sub-exposure-group analyses that were based on only 2 data points. Thus caution must be taken in drawing inferences for the subgroup summaries based on these small numbers. Second, we only estimated crude ORs for the WTC exposure variables without adjusting for other factors, such as age, sex, socioeconomic status, and co-morbidity, which have been shown to affect PTSD outcomes [31,32,36,37]. While changes in the summary ORs may be limited, as the significant associations were still present after adjusting for relevant covariates in most studies included in this meta-analysis, influences of these potential moderators and others that were not considered in the current study deserve further attention by ongoing WTC studies. Third, there was a modest overlap in the WTC-HP and Registry samples, and potentially among studies from the same data source. We attempted to minimize the impact of the shared sample by careful selection of studies and sub-analyses, which produced findings that were comparable to the overall results of the meta-analysis. Finally, the studies reviewed here relied on a self-reported PTSD symptom scale rather than diagnostic interviews, and volunteer samples. We note that the Stony Brook site of the WTC-HP found comparable prevalence rates for PCL>50 and diagnostic assessment of PTSD, and good sensitivity and specificity [38] . While the samples are volunteers, they are large and diverse, and thus the findings are based on broadly obtained symptom and exposure data assessed at varied time points since 9/11. Nevertheless, memory for traumatic event is not fixed and caution must be taken in assessing the accuracy of the recall for traumatic events and the subsequent relationships between stressors and PTSD [39].

Conclusions

Our meta-analysis of ten studies demonstrates significant positive associations between the WTC exposure and probable PTSD across six common exposure categories and the two major cohort types examined. The strength of the associations appeared to be lower among responders as compared to civilians. This difference was more pronounced for physical compared to psychosocial exposure types, suggesting while professional experience and training played an important role in predicting PTSD, other factors may also influence the risk of PTSD, such as heterogeneity of the exposure classification, data source, PTSD cut-point, lapse time since 9/11, as well as differences in sociodemographic profiles.

We also found that injury, lost someone, and witnessed horror were the three strongest predictors of probable PTSD among those affected by the 9/11 terrorist attack, regardless of cohort types. Given the consistency of this finding across populations, patients seeking treatment for 9/11 associated health problems should be asked about experiences of injuries, losses, and witnessing of horror as part of their assessment and providers should be aware of the long-term effect of these exposures on PTSD so that appropriate interventions can be offered. Emergency preparations for future disasters should anticipate these three specific exposures as potential risk factors of persistent PTSD symptoms in both responders and civilians.

Finally, the search resulted in surprisingly few studies met our criteria for this meta-analysis. This scarcity of data highlights the challenge of conducting post-disaster health assessment (sometimes based on quickly developed questionnaires that are prone to lack of compatibility among studies) and the challenges inherent in subsequent services and research efforts to understand both short- and long-term health effects. Thus, psychosocial surveillance techniques such as questionnaires that are able to distinguish between the nature and severity of exposure types should be developed in advance to improve the consensus in the assessment of specific exposure and health endpoints. We also recommend that future studies of WTC responders and civilians provide more specific information on exposure and mental health outcomes so that meta-analyses of long-term effects can encompass a broader array of studies in order to develop and modify existing response and recovery plans, and to prepare and mitigate for future disasters.

Supporting Information

Figure S1 Forest plot of odds ratios (and 95% confidence intervals) of self-reported PTSD risks associated with four specific WTC exposure types common between the responders and civilians. The effect size analysis was based on a subset of data, and showed similar results to those found using the full data set. Notes: Individual ORs from the original studies, summary ORs for the exposure subgroups, and the overall OR were presented. Details of the study numbers (a–j) and cohort types were defined in Table 1. IDs corresponded to a unique internal identification of ORs used in the analysis as shown in Table S1.
(TIFF)

Figure S2 Forest plot of odds ratios (and 95% confidence intervals) of self-reported PTSD risks associated with five specific WTC exposure types among the responders. The effect size analysis was based on a subset of data, and showed similar results to those found using the full data set. Notes: Individual ORs from the original studies, summary ORs for the exposure subgroups, and the overall OR were presented. Details of the study numbers (a–j) and cohort types were defined in Table 1. IDs corresponded to a unique internal identification of ORs used in the analysis as shown in Table S1.
(TIFF)

Figure S3 Forest plot of odds ratios (and 95% confidence intervals) of self-reported PTSD risks associated with four specific WTC exposure types among the civilians. The effect size analysis was based on a subset of data, and showed similar results to those found using the full data set. Notes: Individual ORs from the original studies, summary ORs for the exposure subgroups, and the overall OR were presented. Details of the study numbers (a–j) and cohort types were defined in Table 1. IDs corresponded to a unique internal identification of ORs used in the analysis as shown in Table S1.
(TIFF)

Table S1 Detailed data (n = 37) extracted from the ten original studies included in the meta-analysis, where sample numbers with and without self-reported PTSD (P+/P-) among those with high WTC exposure vs reference levels (low or no) exposure were shown. A subset (*, n = 25) of data was used to further investigate the impact of shared sample issues. Similar results were found for effect size analyses based on both data sets.
(DOCX)

Checklist S1 PRISMA checklist.
(DOC)

Author Contributions

Conceived and designed the experiments: BL HK. Performed the experiments: BL LHT. Analyzed the data: BL LHT. Wrote the paper: BL EJB LHT HK.

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Appendix 4. WTC Bias Analysis proposal

RESEARCH STRATEGIES
SIGNIFICANCE

Bias is one of the most significant challenges in epidemiology, especially in observational studies where avoiding all bias is nearly impossible. Bias is by definition the difference (error) between the measurement and the truth. Avoiding and controlling these biases are usually viewed as the overall goal of epidemiology. Nevertheless most epidemiologic analyses either assume that error is absent or, if present, that errors are random. For example, most conventional statistical methods require the strong assumption that the data were generated in a randomized experiment with perfect compliance. These methods include chi-square test, t-test, and most type of regressions. When this assumption is incorrect the interpretation of "statistical significance" can be highly misleading. While epidemiologic studies often discuss the potential sources and effects of bias (commonly three types: selection bias, information bias, and uncontrolled confounding), the impacts of these biases on study findings are rarely quantified. One of the main reasons for not quantifying bias is because the process requires specifying values (bias parameters) when little or no data are available and often requires advanced statistical techniques such as multiple simulations. The failure to account for the effects of bias can distort study findings and lead to incorrect conclusions about causal inference. Among over 400 publications studying WTC health effects (http://www.cdc.gov/niosh/topics/wtc/science.html), none attempted to systematically identify the presence of bias and assess the potential magnitude of the effects. The proposed study will investigate the potential impacts of three types of bias (selection, information, and confounding) within the WTC responder cohort data. We propose to focus our investigation on four health outcomes (sinusitis, asthma, sarcoidosis, and post-traumatic stress disorder (PTSD)) that have been reported to occur at elevated rates among the WTC responders. We propose to evaluate already-recognized biases in these data and to identify additional potential biases that may not have been previously reported. Further we will quantify how mixed or combined bias effects may be different from those that would be expected from biases acting alone. We will employ the most recent and advanced method for bias modeling, multiple-probabilistic bias analysis (Greenland 2005, Lash 2010) for the four selected health outcomes. The results will present estimates of the impacts of identified biases on the rates of disease for the four health outcomes, and will provide valuable lessons for further investigations of this disaster and future extreme events.

Health surveillance of the WTC responders has the primary goal of identifying health outcomes that have resulted from the exposures suffered at the WTC. To date, a number of health outcomes have been reported to occur more frequently in different groups of WTC responders (Kim 2012, Wisnivesky 2011, Herbert 2006). An important step in the process of deciding which if any of these outcomes is caused by WTC exposures is an assessment of the biases that may have occurred in the assessment of that specific outcome. Each health outcome may have been impacted to different degrees by different biases. Thus to make this investigation practical, we propose to study four specific health outcomes: sinusitis, asthma, sarcoidosis, and PTSD. Sinusitis is a largely reversible and short-term effect that is probably often self-medicated and may be difficult to recall. Sinusitis and asthma have been reported to be found more frequently among WTC responders (Wisnivesky 2011). Asthma is a more serious disease than sinusitis, and probably more frequently receives medical attention and medications. This increases the likelihood that it will be accurately recalled, although the date of onset, which is critical to attributing a case to the exposures of 9/11, may not be remembered accurately. One study has reported "sarcoid-like" granulomatous lung disease in WTC responders (Crowley 2010). This is potentially a very serious disease, presumably chronic, and diagnosed by clinical exam and radiography rather than self-report. Thus the potential biases that might affect this finding are very different from those for the previous two diseases. PTSD is the most frequently reported mental health consequence among responders (Wisnivesky 2011, Luft 2012). The potential biases for this effect are once again different, as the diagnosis is necessarily based on self-report. By studying these four diverse health endpoints, we propose to evaluate a wide range of different types of bias. And the results will have broader applicability than if a single endpoint were studied.

INNOVATION

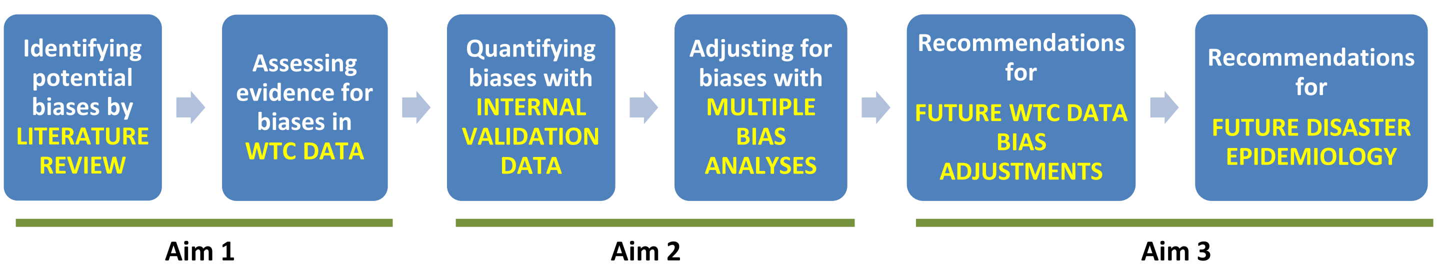
Probabilistic bias analysis is a method to correct for bias and take into account uncertainty about bias parameters (Greenland 1998, Lash 2009). This approach is superior to conventional sensitivity analysis because the former but not the latter explicitly accounts for uncertainty in the bias parameters. Multiple-probabilistic bias analysis provides flexibility to specify a variety of probability density functions (PDF) for the bias parameters and use these PDFs to simulate the range for the bias-adjusted effect estimates. Through this whole process, we aim to estimate the health impacts of the WTC disaster on the responders as closely as possible to the true impacts. By developing recommendations to validate WTC data through validation methods using both internal and external validation data, and by providing detailed protocols for statistical bias adjustment using the WTC responder cohort data, we will assist other researchers in drawing plausible conclusions. Furthermore, our findings can help disaster-based cohorts in the future to avoid bias at the stage of study design.

Multiple-probabilistic bias analysis is now readily available to researchers in widely-used statistical software packages, including Stata. Strengths and benefits of this method have been discussed in various publications (Lash 2009, Orsini 2007, Greenland 2008, 2005).In brief, it allows for uncertainty of the bias parameters and controls for multiple biases in a single model, so that combined effects of several biases can be simultaneously assessed.

We hypothesize that formal bias adjustment may be even more important in disaster epidemiology than in conventional studies because the humanitarian imperative of “medical response first, epidemiology later,” will almost always mean that the resulting data will contain limitations that a carefully planned study could avoid. At the same time, it is another characteristic of disaster studies that the data are irreplaceable – another, better study cannot be done. As a result, we suggest that the methods we propose here may become a necessary and fundamental aspect of all future disaster epidemiology studies.

APPROACH

We propose three major steps to evaluate the impact of bias in the WTC responder cohort. In **Aim 1**, potential biases reported by other investigators will be identified from a review of the currently available WTC health studies literature. We will then look for evidence consistent with each of these biases within the WTC data collected from the monitoring and treatment program. In **Aim 2**, we will develop estimates of the plausible magnitudes and directions of the biases for which strong evidence is identified in Aim 1. We will then use these data in multiple bias analyses to develop ranges of estimates of the disease rates for each of the four health outcomes we are investigating. Finally in **Aim 3**, we will make recommendations for handling bias in additional studies in the WTC responder cohort, and summarize lessons learned from this investigation about how bias analysis can improve future disaster epidemiology studies.



Aim 1. Identify potential biases and use the WTC cohort data to provide evidence of the strength and direction of these biases in the use of WTC responder cohort data

a)Literature review: We will perform a systematic literature review of over 400 published articles about WTC responders (see: http://www.cdc.gov/niosh/topics/wtc/science.html) focusing on those that include analyses of health outcomes using the WTC responder cohort. Our review method will involve a systematic evaluation of selected literature using a set of criteria to determine potential biases. We will first focus on the potential biases identified and discussed by the authors and then add additional unidentified potential biases based on disaster cohort by reviewing major recent disasters including Fukushima Daiichi nuclear disaster, the Deepwater Horizon, Hurricane Katrina, etc. All research articles selected will be reviewed independently by two researchers randomly assigned out of three. The reviewers will determine the likelihood of potential biases for each study. Disagreements, if any will be resolved by discussion with the third reviewer. Bias information from the literature review will be coded within the following categories: study design, type of study measure, main outcomes, and summary results. We will generate a summary table listing the major types of epidemiologic biases (selection, information, and uncontrolled confounding) with specific examples of potential sources of each bias for each study reviewed.

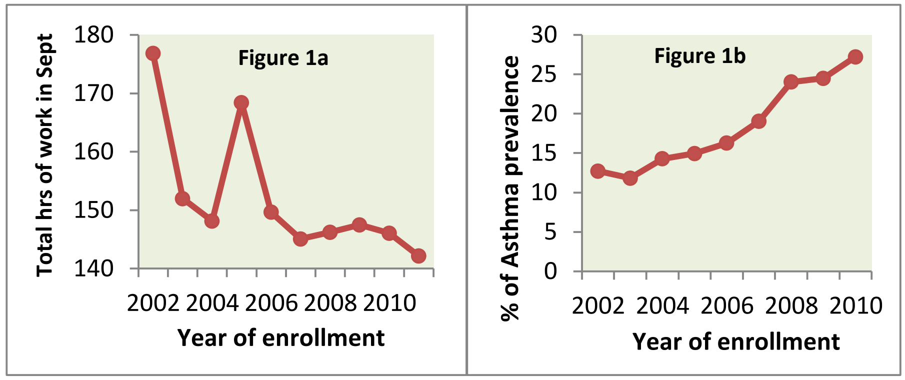


Figure 1a. Total hours of work at the WTC site in 09/2001 by year of enrollment
Figure 1b. Prevalence of asthma by year of enrollment

b) Utilizing WTC responder cohort data: There are several different ways that we can observe evidence suggestive of different biases within the existing data. Although we cannot "prove" or "disprove" the existence of a bias, nor measure it precisely, we can develop more or less evidence suggesting that it probably is/is not acting in studies of a particular health outcome, and we will sometimes be able to find evidence strongly suggesting the direction and plausible magnitude of a bias. Examples are described below. As part of our currently funded WTC research project (1U01 OH010399-01), we have created a dataset that links individual health outcomes, WTC exposures, demographics, occupational characteristics, and program enrollment and follow-up visit participation history. This linked and cleaned dataset is a very valuable resource for the proposed studies. Preliminary examination of potential biases in these data has shown the need for the more systematic analyses proposed in this study. Some of these preliminary findings are summarized here.

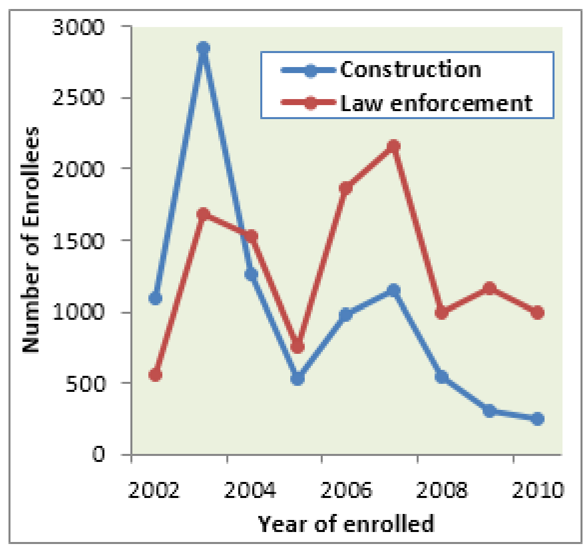


Figure2. Number of enrollment by year between construction and law enforcement workers

Selection bias: As an open cohort, (into which eligible responders could enroll or drop out at any time from its inception in 2002 till the present), a variety and evolving set of factors may have influenced who enrolled and who was retained over time. From the inception of the program (2002) to 2011, slightly over 30,000 WTC responders voluntarily enrolled in the program, while the total number of eligible responders has been estimated to be anywhere from 40,000 (Savitz 2008) to 91,469 (Brackbill 2006, Murphy 2007). Among several exposure variables currently available, we found that responders who enrolled in 2002 reported more work hours at the WTC site in September 2001 than those who enrolled later. As time elapsed, the number of work hours at the WTC site decreased gradually (except in 2005) (Figure 1a). We compared this trend in exposure levels to the asthma prevalence over time. Interestingly, the opposite trend was observed (Figure 1b). Other respiratory symptoms showed the same trend. This pattern could result from changes in selection bias over time such that sick responders may have become more likely to enroll over time, or it could result from a cumulative effect from a longer observation period. In any case, it is a clear example of selection bias that systemically leads the association towards the null because the more highly exposed (who enrolled earlier) reported lower asthma prevalence.

Sample bias: Selective outreach activity or selective recruitment by occupation can add a more complex type of selection bias. Nearly half (44%) of construction workers enrolled in the program between 2002 and 2003, while only 25% of law enforcement workers enrolled during the same time period, and 43% of law enforcement workers enrolled between 2006 and 2008 (Figure 2). This disparity happened because NYPD was actively recruited from 2005, while construction workers were more actively recruited in the beginning of the program. Since law enforcement workers were more likely to enroll later in the program and construction workers earlier in the program, it may be difficult to determine whether differences in outcome rates result from differences in exposure or differences due to the time of enrollment. To explore this further, we calculated the percent difference in sinusitis incidence between law enforcement (enrolled more in later years) and construction workers (enrolled more in earlier years), and we observed more sinusitis among law enforcement workers over time (Figure 3).

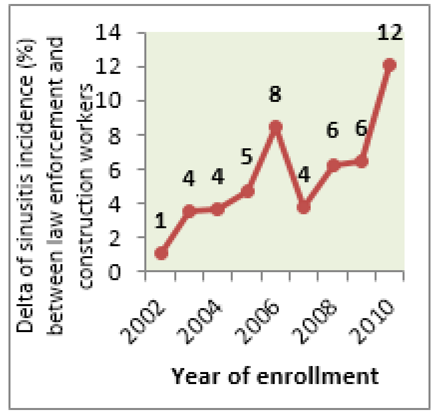


Figure3. Percent difference of sinusitis incidence between law enforcement and construction workers (*Delta=% sinusitis incidence of law enforcement -% sinusitis incidence of construction*)

Recall bias: The delay from event to recruitment varied with the different waves of recruitment. This likely leads to differing levels of recall with time, and so as noted above with other aspects of the recruits, like occupation, and possibly also disease severity. Figure 4 shows percent of missing data for the date of diagnosis from seven different health outcomes during the enrollment examination. Date of diagnosis is critical information in order to calculate incidence rate. In figure 4, the rates of missing date of diagnosis were lower than 5% until 2007, and then jumped to over 10%. The trend of missing the date of diagnosis showed a fairly clear exponential pattern overtime. The pattern was also somewhat non-differential by different health outcomes regardless of the severity (i.e., sinusitis (mild) vs. sarcoidosis (severe)). This same pattern of missingness was observed with some exposure data such as frequency of using mask or respirator, hours of work, etc.

Confounding: None of the WTC studies to date have systematically controlled for general occupational exposures apart from the WTC exposures. Because most of the responders performed tasks at the WTC site that were the same or similar to their regular job (Woskie 2012), and also continued that same job after their work at the WTC site was over, not controlling for this can distort the effects of WTC exposure in both directions: away from or towards the null. Background occupational exposures can add more cumulative effect to WTC exposure, but also might reduce WTC exposures because responders may be prepared to protect themselves from WTC exposures with use of proper personal protective equipment and training. In fact, we found that 66% of asbestos workers reported that a fit-test for a respirator was performed when the respirator was used, but only 23% of police reported performing a fit-test when the respirator was used. This may indicate less WTC exposure among asbestos workers because they used the proper personal protective equipment, but they may have a higher cumulative exposure from their regular job, in addition to WTC work.

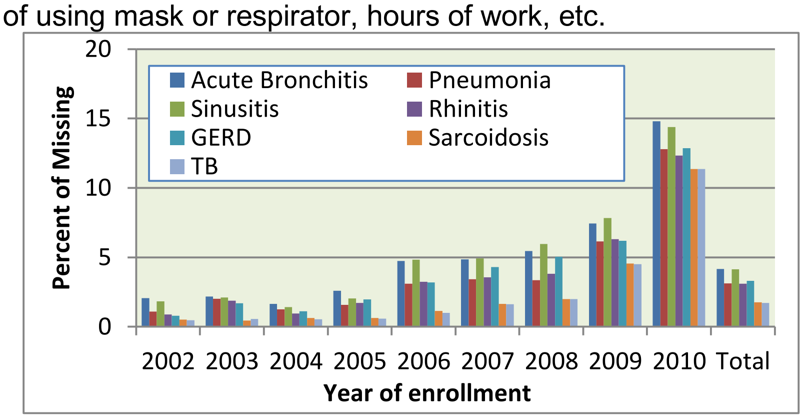


Figure 4. Percent of missing in date of diagnosis by year of enrollment

Aim 2. Quantify the effects of the likely biases on the risk estimates for the four proposed health outcomes, and produce bias-adjusted estimates of the effects of various WTC exposures on health outcomes

In this step, the important biases identified in Aim 1 will be quantified and their impacts will be adjusted. Quantification will use several different approaches whose applications to epidemiologic data are increasingly common (Greenland 2005, Pearce 2007, Lash 2009, Gustafson 2010, Dohoo 2013). As noted, the presence/absence, direction and strength of each bias will vary for each study hypothesis- all of which have the general form:"High level of WTC exposure X increases the rate/risk of health outcome Y". For this reason, the bias analysis will be performed for each of four health outcomes and each type of bias.

a) Internal-validation data with repeated measures: Because the WTC responder cohort is a longitudinal design with repeated examinations every 12-18 months, data on most health outcomes and some confounders have been collected several times. These repeated measures can be used for internal validation of errors, specifically missing and unmatched values across visits. These errors can be replaced with more valid data which might include for example two or more matched values from multiple visits. We are awareof the possibility that even matched data may not be valid if another bias was involved. However, because no gold standard is currently available or hard to obtain without re-interviewing responders, we will generally assume that matched values across visits are valid for these analyses. Through this approach, we will test bias that occur from missing and unmatched values among the four health outcomes. After replacing missing and unmatched values, we will use the Heckman selection model (Heckman 1979) to quantify and adjust specifically for sample selection bias that arises from differential missingness within levels of covariates. The specific steps are:

1) *Quantify the amount of error without replacement using valid data (matched values across visits)*
2) *Replace error when valid data are available (requires 3 or more visits)*
3) *Quantify the amount of remaining error after replacement with valid data*
4) *Using Heckman's selection model, check the randomness of the remaining error within levels of exposures and confounders.*
5) *If the error is random, conclude no bias exists*
6) *If the error is systematic, then obtain adjusted estimates from the Heckman model.*

The above process has two levels to treat error. The first replaces missing or unmatched values with other matched values from the individual under the assumption that matched values are valid. This is a direct repair of error regardless of whether the error is random or systemic. However only 50% of participants made three or more visits in this cohort, the other half of the study population does not have internal-validation data. Therefore another way to treat the remaining error is needed. The second confirms randomness of the remaining error, and quantifies and adjusts for the bias if the error is not random (systemic). The Heckman selection model will be used to test the randomness of error among selected covariates. Heckman's model assumes that there exists an underlying regression relationship, $Y1_i = b_i{*}X_i + e1.$ However when the dependent variable has missing observations, the observed values in the dependent variable are conditional to $Y2_i = g_i{*}Z_i + e2,$ where X_i is a vector of determinants of $Y1_i$, Z_i is a vector of determinants of $Y2_i$, and $e1$ and $e2$ are random error terms for each X_i and Z_i. The earlier equation is a basic regression equation to predict only observed dependent variables and the latter one is the selection equation that predicts unobserved dependent variables. We will fit four separate models for the four health outcomes using WTC exposure variables, such as arrival time at the site, while adding a set of variables (Z_i) thought to determine whether the dependent variable is observed or unobserved. This latter set of variables (Z_i) will be chosen from among data on WTC exposures, demographics, occupational history, confounders (such as smoking and alcohol consumption history), enrollment and participation records, and other health outcomes.

b) Bias modeling using multiple probabilistic bias analysis: Although Heckman's selection model adjusts for bias and quantifies its effect, this method is applicable only to "sample selection bias" that arises from missing dependent variable values (Heckman 1979, Cameron 2009). To extend bias analyses to other types of bias, we will use methods that consider the impact of bias as a distribution of values, a random factor instead of a fixed parameter. These methods improve upon the primary limitation of deterministic sensitivity analyses (simple or conventional sensitivity analysis) which lack explicit accounting for uncertainty about bias parameters (Greenland 1998). The most recent method to implement bias analysis with random bias parameters is probabilistic bias analysis. Although this analysis can be performed using SAS, Stata, and BUGS, Stata implements a program specifically for probabilistic bias analysis, called "*episens*" (Orsini 2008). The technique involves three steps using Monte Carlo simulation: 1) Drawing a random sample of a set of bias parameters from the specified probability density function (PDF); 2) Back-calculating a bias-adjusted effect estimate from the drawn parameters; and 3) Repeating these two steps over time to obtain a distribution of bias-adjusted effect estimates. This process iterates tens of thousands of times to obtain accurate descriptions of the distribution of the bias-adjusted effect estimates. Single bias effect will be quantified by calculating single bias-adjusted effect estimates, and then multiple bias effects will be quantified using multiple bias modeling. The multiple adjustments will be done in this order: 1) adjusting for misclassification of the exposure, 2) adjusting for selection bias, and 3) adjusting for uncontrolled confounding. To perform this analysis, the following bias parameters must be defined by the researcher:

- For **misclassification of exposure:** *sensitivity* and *specificity* among cases and non-cases, respectively
- For **selection bias:** *selection probability* among cases exposed/unexposed and non-case exposed/unexposed
- For **uncontrolled confounding**: *prevalence of confounder* among the exposed and unexposed

Each of these bias parameters will be obtained from Aims 1 and 2 by utilizing the WTC data and literature review. For example, true positives and negatives that are required to estimate sensitivity and specificity can be obtained either from repeated measures or other studies with better assessment of subsamples of WTC responders. Selection probabilities can be obtained from comparing exposure probabilities between loss to follow-up cases and surviving cases. If the confounder was measured, but not controlled, the prevalence can be directly obtained from WTC data. If the confounder was not measured, then the prevalence can be obtained from other studies reporting the confounder. Even with the best efforts to obtain these parameters as close as possible to their "true values", uncertainty will remain, and so the proposed probabilistic methods will produce the most honest estimates of the ranges of effects, taking account of the several different uncertainties that this proposal targets.

As an example of the approach we propose, we have demonstrated adjustment for a single source of error, exposure misclassification, using probabilistic analysis in these data created in our current U01 WTC grant. We found a cumulative incidence of 13% for new onset arthritis among a subset (n=24,000) of the entire WTC data. Exposure was defined and dichotomized according to the worker's arrival time at the WTC site (exposed=arrived on 9/11 AM, unexposed=arrived after 9/11 AM). We treated the data as cross-sectional in this example for simplicity. The risk ratio (RR) of arthritis incidence was not significant at alpha=.05, although elevated (RR=1.06, 95% CI=0.98-1.15). This may be due to misclassification of arrival time. For this example, we assumed that sensitivities and specificities of arthritis reporting among cases and non-cases followed trapezoidal distributions (a distribution with a low and upper limits and a high probability middle range) and ranged from 0.7 to 1 with intermediate interval values between 0.8 and 0.9. In the real analysis, each bias parameter will be obtained based on the best available information from the literature, utilizing existing data, and previous research. The data for this example was analyzed using the "episens" program in STATA and it generated bias adjusted point estimate with 95% adjusting for systematic error only and both systematic and random errors. In this analysis, arthritis significantly increased among those who arrived early at the WTC (RR=1.14, 95% CI=1.07-2.96) after adjusting for systematic exposure misclassification. Adjusting for both systematic and random misclassification, the RR was practically the same but the 95% CI became wider (RR=1.16, 95% CI=1.02-2.93). Similar bias analyses will be performed to control for all three types of bias identified through Aim1 for the four health outcomes. Although not covered in this example, after single bias adjustment, multiple biases adjustment will be performed to demonstrate the simultaneous effect of multiple biases.

Aim 3. Develop recommendations for bias adjustment in WTC health studies and future disaster studies

As noted above, disaster epidemiology has several unique attributes that distinguish it from normal epidemiologic research. Perhaps most fundamental is the reality that the first priority will always be for health care, with health surveillance following with some delay. On top of this, the resource constraints and time pressures create opportunities for errors in data collection that should normally be avoided through careful planning, piloting of survey instruments, systematic or random sampling of participants, etc. A broad hypothesis of this research is that systematic bias analysis should always be an essential component of disaster epidemiology, because of these inherent constraints. In Aim 3, we propose to synthesize and disseminate lessons learned from this study, **applying research to practice** at two levels: within the universe of future additional health studies of the WTC responders, and more generally in future disaster epidemiology.

We will develop **recommendations for bias adjustment** in three steps. **First**, a systematic method to identify biases will be developed through Aim1. The method will be a user-friendly version that includes Stata programming that researchers can use to easily and quickly obtain statistical evidence of bias. **Second**, recommendation for bias correction using internal-validation data will be created. There are various types of internal-validation data available including repeated measures, as we proposed in Aim 2a, and clinical confirmations such as blood test, x-ray, MRI, biopsy, etc to confirm self-reported health outcome. We will review the WTC database to explore what validation data are available and determine the best validation data to use. In addition, a sub-sampling method will be provided when no validation data are available. This method will guide researchers to select random sub-samples within the cohort and validate the entire cohort data using the sub-sample. **Third**, a detailed and systematic statistical method to adjust identified biases will be provided. Through Aim2, we will create Stata programming for each bias that can be applicable in other health outcomes besides the four health outcomes we selected in this project.

For **future disaster epidemiology**, we will develop a guide to reduce biases at the stage of study design. Once a study has begun to collect data some sources of bias may be unavoidable and the bias adjustment methods we propose should be applied. In this guide, the unique situations that can be created by various disasters will be considered and the biases that may be produced will be described along with methods for adjustment. These two products will be disseminated via peer-review journals, technical reports, WTC PI meetings, and scientific conferences.

Appendix 5.

TITLE: Lowered socioeconomic status among WTC responders and mediation effect of asthma incidence

AUTHORS: TBA

ABSTRACT

Among the 26,768 responders who participated in the WTC Health Program by December 31, 2010, 32% (n=8,531) of the responders who held a full-time job at the baseline visit (visit 1), participated in at least one follow-up visit, and had information regarding an asthma diagnosis were included in this analysis. Among participants, 39% (n=2,936) maintained full-time status through the last visit and 61% changed job status (n=5,159) at a follow-up visit. Examining responders who changed job status, 39.7% changed to part-time, 8.5% became disabled, 15.3% were laid-off, and 36.5% were retired. In fully adjusted models, upon comparing change in job status by asthma diagnosis, asthmatics were 14% more likely to experience a change in their full time status compared to non-asthmatics. In particular, asthmatics were 86% more likely to become disabled and 21% more likely to retire than non-asthma cases. In stratified analyses, while participant demographics and WTC-related exposures influenced job status change among non-asthmatics, within asthmatics only the type of respiratory protective equipment used was associated with job change. Our findings suggest that changes to socioeconomic status as a result of job loss should be considered an important adverse consequence of WTC exposure, especially among responders who have developed health problems. Assistance with maintaining full-time job status is recommended among WTC responders who developed health problems (e.g. asthma), as well as those that have not yet developed health problems, but were exposed to WTC.

BACKGROUND

Asthma is a chronic lung disease which affects approximately 26 million children and adults in the United States each year. Along with the burdens on the healthcare system, uncontrolled asthma poses severe economic and social consequences as well, including missed work days and lost productivity and earnings. A recent national study observed that medical expenditures were up to $4423 greater among individuals with uncontrolled asthma and were more likely to be unemployed, be absent from work and have more activity limitations compared with those who did not have asthma (Sullivan et al., 2014). Work-related issues due to asthma have also been found to quality of life including beliefs that asthma had adversely affected their career by causing workers to: not pursue a desired career; not get promoted due to absenteeism; change to a worse job; and be perceived as incapable of more responsible assignments (Mancuso et al., 2003).

Among asthmatics employed in the workforce, recent studies have found that the negative socioeconomic consequences of asthma are mostly influenced by professional and demographic factors, including reduced possibilities for relocation to an unexposed job within the same company, lower levels of education, and lack of effective retraining programs (Vandenplas, 2008). Additional studies of asthmatics found that blue collar workers having either asthma or chronic obstructive pulmonary disease were less likely to return to work quickly compared with office workers and asthmatics working in smaller companies had higher unemployment rates (Peters et al., 2007).

The collapse of the World Trade Center (WTC) towers on September 11, 2001 exposed a large number of first responders and nearby residents to the potential toxic effects of multiple airborne pollutants. Multiple health problems related to WTC exposures have been documented in the literature; in particular the increased prevalence of respiratory symptoms and diagnoses such as asthma and reactive airways dysfunction syndrome (Kim et al., 2012; Wheeler et al., 2007; Feldman et al., 2004; Landrigan et al., 2004). Recent studies have also observed an increased rate of asthma and other pulmonary disorders among certain groups of WTC responders, such as firefighters (Aldrich et al., 2010). Although high rates of asthma symptoms among WTC responders have been reported and asthma has been associated with decreased work productivity and lowered quality of life, the impact of asthma on work outcomes among WTC responders has not been investigated.

In this study, we used data from a prospective cohort of responders participating in the WTC Medical Monitoring and Treatment Program between 2002 and 2010 to assess whether responders diagnosed with asthma after exposure to the WTC disaster experienced greater reduced work productivity compared with responders not diagnosed with asthma.

METHODS

Study Population

The study population consisted of 25,670 responders who participated in the WTC Health Program by enrolling in one of the five WTC clinical centers (NY/NJ WTC consortium) at least once between July 16th, 2002 and December 31st, 2010. The WTC Health Program initially started as a medical screening program of workers and volunteers who worked at the WTC sites (lower Manhattan, the Staten Island landfill, barges and loading piers) for at least 4 hours from 9/11 to 9/14, 2001, at least 24 hours in the month of September, or at least 80 hours from 9/11 to the end of December 2001. Additional workers who were eligible included morgue workers and employees of the Office of the Chief Medical Examiner (OCME) and the Port Authority Trans-Hudson Corporation workers (Herbert 2006). Active firefighters and emergency medical services (EMS) workers of the Fire Department of the City of New York (FDNY) were served by a separate but similar health surveillance system -- the FDNY WTC Health Program and are not included in this analysis.

The study cohort consisted of responders who participated in the WTC Health Program by December 31, 2010, who held a full-time job at the baseline visit, and participated in at least one follow-up visit. Participants underwent a comprehensive baseline interview and were subsequently followed every 12-18 months for periodic exams and data collection regarding current job status. Among the 26,768 responders who participated in the WTC Health Program by December 31, 2010, 32% (n=8,531) were included in the analysis.

Asthma and Job Status Information

To ascertain asthma diagnosis, participants were asked if they were ever diagnosed by a doctor as having asthma or history of reactive airways dysfunction syndrome. WTC responders were also asked to report the date of their asthma diagnosis, as well as whether they had an asthma attack during the prior 12 months. To distinguish lifetime prevalence of asthma versus incident asthma, participants who reported history of an asthma diagnosis prior to January 2002, were not included as incident asthma cases.

During baseline and follow-up interviews, participants were also asked several questions related to employment status and occupation. Employment status was categorized as the following: (1) full-time, (2) part-time, (3) disabled (due to WTC or non-WTC exposure), (4) laid off or unemployed, (5) retired, student, or other.

Information on WTC dust exposures

WTC exposures were also assessed using an interviewer administered questionnaire. Among the various exposure variables collected, we selected four major WTC exposures that potentially indicate the level of WTC dust/fumes. First, arrival time to WTC site categorized as1) arrived on 9/11 in the dust cloud, 2) arrived on 9/11 not in the dust cloud, and 3) arrived on 9/12 or later. Second, number of hours worked at WTC site in September as a continuous variable. Third, location of work performed in September categorized as 1) on the pile or in the pit, 2) adjacent to the pile or the pit, 3) landfill, 4) barges or loading piers, and 5) elsewhere, south of Canal St or the Office of the Chief Medical Examiner at 520 First Ave in Manhattan. These three WTC exposures have previously been described in detail (Woskie 2011). Lastly, we included the type of respiratory protection equipment used in 9/11-9/18 as three categories 1) did not wear one, 2) nuisance dust/surgical/disposal masks, with a N95 to P100 rating at most, and 3) half-face or full-face respirator with replaceable filters/chemical cartridges/clean air supply (SCBA)/powered air purification (PAPR) (Antao 2011).

Additional covariates

Additional covariates include age at baseline visit, sex, race and ethnicity (categorized based on the Office of Management and Budget classification), income, marital status, and cigarette smoking. Age at baseline visit was grouped into the following categories: 18-29, 30-39, 40-49, 50-59, and >60 years of age. Highest level of education received was categorized into less than high school, high school or equivalent, more than high school, and missing.

Pre-9/11 occupations were identified by asking "what was your trade/profession on 9/10/01?" Narrative text of this occupation has been cleaned and re-categorized using the Standard Occupational Classification (SOC) 2000 developed by the Bureau of Labor Statistics (BLS, 2015). Five major categories were used: 1) construction workers (SOC code: 47-000), 2) protective service workers (33-000), 3) electrical, telecommunications, & other installation & repair workers (49-000, abbreviated to "utility" from here,), 4) Transportation and material movers (53-000, abbreviated to "transportation" from here"), and 5) business, engineering & administration (11-000, 13-000, 17-000, abbreviated to "business" from here). Additional details of pre-9/11 occupation have been previously reported (Woskie 2011).

Statistical Analyses

The χ^2 test was used to compare the distribution of baseline characteristics by employment status among WTC participants. To examine the effect of asthma diagnosis on change in job status, a series of generalized estimating equations (GEE) were calculated with a 95% confidence interval (CI) based on the Poisson distribution. To handle mild violations of the equidisperson assumption (underdispersion) of the Poisson distribution when the outcome variable is a binary or count response, the robust variance option in Stata was used (Cameron 2009). Unadjusted and adjusted models examining the association between asthma diagnosis and any change in job status (yes/no) was first modeled, with subsequent models examining the effects of asthma diagnosis on the type of change in job status, (1) from full time to part time, (2) full time to disabled, (3) full time to retired, and (4) full time to laid off. Analyses were performed with Stata 12.0 (Stata Corp., College Station, TX). To determine whether the distribution of demographic and WTC dust exposures differed based on asthma diagnosis, stratified models examining risk factors associated with job change were conducted among asthmatics and non-asthmatics.

All analyses were performed using Stata software version 11.2 (StataCorp LP). The study was approved by the Institutional Review Board of the Feinstein Institute for Medical Research at the North Shore-LIJ Health System and only participants who provided signed consent to use their data were included in this study.

RESULTS

Descriptive Characteristics

Overall 8,531 WTC responders were included in the study cohort. Mean age of WTC responders was 42 (± 8 years). Eighty seven percent were males, 62% were White, 11% Black, and 23% were of Hispanic ethnicity. The most common occupations were protective services (57%), construction (12%), and other (15%). Eight percent of WTC responders were diagnosed with asthma within the 2002 to 2010 follow-up period. Among participants, 39% (n=2,936) maintained full-time status through the last visit and 61% changed job status (n=5,159) at a follow-up visit. Of responders who changed job status, 39.7% changed to part-time, 8.5% became disabled, 15.3% were laid-off, and 36.5% retired, became students, or listed other employment status.

Results of Multivariable Models

Table 2 displays the results of the multivariable models examining the associations between asthma diagnosis, WTC-related exposures, and change in job status among participants. In fully adjusted models, responders who received an asthma diagnosis had a 14% increased risk of experiencing a negative change in job status compared to non-asthmatics (IRR 1.14, 95% CI 1.03-1.25). In particular, asthmatics were significantly more likely to experience a negative change in job status as a result of disability or retirement, when compared to non-asthmatic responders (IRR 1.86, 95% CI 1.30-2.65 and IRR 1.21, 95% CI 1.02-1.44 respectively).

Responders of Hispanic ethnicity were significantly less likely to experience job change when compared to non-Hispanic Whites, while women experienced more job change than men particularly, retirement. Among WTC responders, those with higher levels of education experienced less job change than responders with less than a high school degree. Responders in the older age categories (30-39, 40-49, 50-59, and >60 years of age) experienced more frequent job change than those in the 18-29 category, particularly change in employment from full time status to retired. Responders within higher income categories were significantly less likely to experience change in job status overall, with the exception of change from full time status to retirement, when compared to responders whom reported income within the less than thirty thousand per year category.

Among various occupation groups, responders employed in protective services were less likely to experience job change, while responders in construction were more likely to experience job change. When compared to responders employed in protective services, responders employed in construction were 2.5 times more likely to experience a job change due to disability and 15 times more likely to be laid off (IRR 2.54, 95% CI 1.76-3.67 and IRR 15.10, 95% CI 10.01-22.8 respectively). Upon examination of WTC related dust exposures, no statistically significant differences in job status change were observed with respect to arrival time to WTC site, total hours worked at the WTC site in September, primary location of work performed in September, or use of respiratory protection equipment.

Results from Stratified Models

Table 3 displays the results of the multivariable models examining the associations between participant demographics, WTC dust exposures, and job status change among asthmatic and non-asthmatic first responders. Among non-asthmatics, sex, race/ethnicity, education, age, occupation, and income were all significantly associated with change in job status. Among non-asthmatics, respondents of Hispanic ethnicity, higher levels of education and income, and those employed in utility jobs were significantly less likely to experience job change. Conversely, among non-asthmatics, women, participants in older age categories, and those in construction were significantly more likely to experience a change in job status. Intriguingly, among participants diagnosed with asthma, the only factor that was associated with job status change was whether the first responder used respiratory protection equipment. Asthmatics who reported using nuisance dust/surgical/disposal masks were significantly more likely to experience a change in job status (IRR 1.41, 95% CI 1.04-1.91).

DISCUSSION

This study investigated the pattern of job status changes from full-time employment to less than full-time among WTC responders and compared the risk between asthmatic and non-asthmatic groups. This topic has not been previously studied among WTC responders, even though lowered socioeconomic status through changes in occupation may have a strong negative impact on quality of life and has been adversely associated with both physical and mental health. We observed that asthma was an independent predictor of job status change, after controlling for demographics and WTC exposures. Responders diagnosed with asthma had a 14% greater risk of losing their full-time job than those without asthma. Notably, asthmatics were 86% more likely to become disabled and 40% more likely to retire compared to responders without asthma. In stratified analyses, while participant demographics and WTC-related exposures influenced job status change among non-asthmatics, within asthmatics only the type of respiratory protective equipment used was associated with job change. These results demonstrate that asthma is likely to be the sole reason participants have lost their full-time job status.

Our study findings evidently demonstrate that WTC responders who developed a new onset of asthma were at increased risk of having a decrease in job status from full-time employment. SES should be considered an important adverse consequence of WTC exposure, especially when lowering SES impacts developing health problems or worsening current problems. Additional programs and outreach efforts are recommended to assist responders who have experienced a decrease in SES, particularly among those who have also experienced health problems.

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Tables

Table 1. Asthma status, demographics, and WTC dust exposures, by job status change within WTC Health Program participants (n = 8,351)

	No Job Change		Any Job Change		p – value
Variables	**n**	**%**	**n**	**%**	
Asthma diagnosis					0.003
Asthmatic	485	9.1	333	11.1	
Non-asthmatic	4856	90.1	2677	88.9	
Sex					0.006
Male	4679	87.6	2573	85.5	
Female	662	12.4	437	14.5	
Race/ethnicity					0.003
Non-Hispanic White	3360	62.9	1941	64.5	
Hispanic	649	12.1	305	10.1	
Non-Hispanic Black	99	1.85	40	1.3	
Asian	157	2.9	70	2.3	
Other/missing	1076	20.1	654	21.7	
Education categories					<0.001
Less than high school	3536	66.2	2135	70.9	
High school or equivalent	1677	31.4	780	25.9	
More than high school	128	2.4	95	3.2	
Income categories					<0.0001
<$30,000	206	3.9	239	7.9	
$30-60,000	2770	51.8	1361	45.2	
$60-80,000	1451	27.2	838	27.9	
>$80,000	914	17.1	572	19.0	
Age categories					<0.0001
18-29	239	4.5	110	3.7	
30-39	2074	38.8	835	27.7	

40-49	2244	42.0	1286	42.7	
50-59	695	13.0	631	21.0	
60 and above	89	1.7	148	4.9	
Occupational categories					<0.0001
Protective service	3097	60.1	1499	51.6	
Construction	551	10.7	443	15.3	
Utility	400	7.8	188	6.5	
Transportation	191	3.7	131	4.5	
Business	203	3.9	113	3.9	
Other	708	13.8	529	18.2	
WTC arrival time					<0.0001
On 9/11 in dust cloud	1131	21.8	627	21.4	
On 9/11 not in dust cloud	1355	26.1	701	23.9	
Arrived 9/12 or later	1701	32.7	866	29.5	
Missing	826	15.9	569	19.4	
Respiratory protection equipment use					<0.0001
Did not wear one	1022	20.6	546	20.5	
Nuisance dust/surgical/disposal	2757	55.5	1374	51.5	
Half-face or full respirator	759	15.3	491	19.4	
Location of work in Sept 2001					
On the pile	1932	36.2	1088	36.1	
Adjacent to pile	2390	44.7	1288	42.8	
Landfill	137	2.6	89	3.0	
Barges/loading piers	53	1.0	38	1.3	
OCME	90	1.7	40	1.3	
Elsewhere South of Canal St	368	6.9	197	6.5	
Don't know/ Missing	371	6.9	270	9.0	
Mean Total hours on site Sept 2001 (95% CI)	148.7	(146.1-151.3)	143.8	(140.25-147.3)	0.03

Table 2. Adjusted associations of asthma diagnosis, demographics, WTC related dust exposures and change in job status among WTC Health Program Participants (n = 8, 351)

	Any Job Change		Full time to part time		Full time to disabled		Full time to retired		Full time to laid off	
Variables	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI
Asthma diagnosis	1.14	(1.03-1.25)*	0.92	(.75-1.12)	1.86	(1.30-2.65)*	1.21	(1.02-1.44)*	1.26	(.91-1.76)
Gender										
Male	REF		REF		REF		REF		REF	
Female	1.58	(1.05-1.27)*	1.01	(.84-1.21)	1.33	(.90-1.96)	1.46	(1.24-1.72)*	0.81	(.56-1.16)
Race/ethnicity										
Non-Hispanic White	REF		REF		REF		REF		REF	
Hispanic	0.81	(.73-.91)*	0.71	(.57-.88)*	0.94	(.61-1.43)	0.85	(.70-1.02)	0.96	(.65-1.42)
Non-Hispanic Black	0.82	(.61-1.11)	0.54	(.29-1.02)	0.35	(.05-2.48)	1.05	(.65-1.70)	1.86	(.85-4.05)
Asian	0.84	(.67-1.04)	0.97	(.69-1.36)	0.34	(.08-1.35)	0.69	(.49-1.08)	1.3	(.70-2.43)
Other	0.98	(.90-1.06)	0.89	(.77-1.03)	1.16	(.83-1.64)	0.82	(.70-96)*	1.52	(1.19-1.94)
Education										
Less than high school	REF		REF		REF		REF		REF	
HS or equivalent	0.81	(.75-.88)*	0.86	(.75-.98)	0.8	(.56-1.13)	0.77	(.69-.88)*	0.79	(.59-1.06)
More than HS	1.06	(.88-1.28)	0.98	(.68-1.42)	1.75	(.98-3.13)	0.89	(.57-1.37)	1.09	(.68-1.75)
Income categories										
<$30,000	REF		REF		REF		REF		REF	
$30-60,000	0.68	(.60-.78)*	0.74	(.57-.96)*	0.56	(.33-.94)	3.55	(1.86-6.78)*	0.35	(.25-.48)*
$60-80,000	0.73	(.64-.84)*	0.81	(.62-1.07)	0.33	(.18-.61)	4.02	(2.09-7.73)*	0.33	(.22-.48)*
>$80,000	0.74	(.65-.85)*	0.87	(.66-1.14)	0.51	(.29-.89)	3.52	(1.82-6.80)*	0.42	(.30-.60)*
Age categories										
18-29	REF		REF		REF		REF		REF	
30-39	1.01	(.83-1.22)	1.1	(.82-1.49)	1.28	(.59-2.77)	2.34	(1.04-5.25)*	0.66	(.45-.99)*
40-49	1.28	(1.06-1.54)*	0.97	(.72-1.31)	1.47	(.68-3.15)	4.5	(2.24-11.16)*	0.89	(.62-1.30)
50-59	1.68	(1.39-2.03)*	0.92	(.66-1.26)	1.92	(.88-4.17)	10.19	(4.52-22.98)*	0.86	(.58-1.28)
60 and above	2.23	(1.80-2.76)*	0.76	(.46-1.26)	1.1	(.35-3.47)	25.68	(11.21-58.83)*	0.43	(.20-.93)*
Occupation										
Protective service	REF		REF		REF		REF		REF	
Construction	1.16	(1.06-1.28)*	1.01	(.83-1.22)	2.54	(1.76-3.67)*	0.41	(.33-.52)*	15.1	(10.01-22.8)*
Utility	0.8	(.69-.93)*	0.94	(.72-1.21)	1.56	(.90-2.71)	0.45	(.34-.60)*	4.08	(2.29-7.25)*
Transportation	1.07	(.92-1.24)	1.1	(.82-1.48)	2.38	(1.40-4.05)*	0.63	(.47-.83)*	5.74	(3.14-10.50)*

Business	0.87	(.73-1.04)	1.14	(0.85-1.55)	1.35	(.66-2.76)	0.42	(.29-.59)*	5.29	(2.75-10.15)*
Other	1.05	(.95-1.15)	1.22	(1.02-1.44)*	1.5	(.99-2.27)	0.38	(.30-.48)*	10.04	(6.65-15.16)*
WTC arrival time										
On 9/11 in dust cloud	REF		REF		REF		REF		REF	
On 9/11 not in dust cloud	0.97	(.89-1.06)	1.02	(.87-1.19)	0.7	(.48-1.03)	0.99	(.85-1.15)	0.96	(.67-1.36)
Arrived 9/12 or later	0.92	(.85-1.00)	0.93	(.79-1.09)	0.73	(.52-1.03)	0.95	(.81-1.11)	0.97	(.71-1.34)
Missing	1.02	(.91-1.13)	1.2	(.99-1.45)	0.6	(.38-.94)*	0.89	(.68-1.09)	1.07	(.75-1.52)
Respiratory protection equipment										
Did not wear one	0.97	(.89-1.06)	1.02	(.88-1.19)	0.76	(.55-1.06)	0.99	(.86-1.15)	0.81	(.61-1.08)
Nuisance dust/surgical/disposal	1.09	(.98-1.20)	1.18	(.98-1.42)	1	(.67-1.50)	0.87	(.71-1.11)	1.16	(.86-1.56)
Half-face or full respirator	1.4	(.92-2.13)	1.1	(.31-3.87)	3.1	(.85-11.26)	1.37	(.54-3.51)	0.99	(.65-1.49)
Location in Sept										
Adjacent to pile	0.93	(.87-1.00)	0.88	(.78-1.00)	0.9	(.67-1.19)	1.01	(.89-1.15)	0.91	(.72-1.14)
Landfill	1.1	(.91-1.33)	0.93	(0.64-1.33)	0.23	(.03-1.70)	1.47	(1.09-1.98)*	1.24	(.46-3.32)
Barges/loading piers	1.19	(.93-1.54)	1.44	(.93-2.21)	1.02	(.33-3.18)	1.07	(.65-1.78)	0.8	(.27-2.43)
OCME	0.92	(.69-1.22)	0.92	(.57-1.49)	0.8	(.20-3.26)	0.99	(.62-1.56)	0.5	(.07-3.30)
Elsewhere South of Canal St	0.93	(.82-1.06)	0.85	(.66-1.09)	0.71	(.38-1.31)	1.14	(.91-1.42)	0.8	(.48-1.35)
Missing	0.9	(.75-1.09)	0.74	(.51-1.07)	1.36	(.68-2.70)	0.99	(.71-1.38)	0.97	(.53-1.78)
Total hours on site	1	(1.00-1.00)*	1	(.99-1.00)	0.99	(.99-1.00)	1	(1.00-1.00)*	1	(.99-1.00)

*p<.05

Table 3. Adjusted associations of demographics, WTC dust exposures, and job status change among asthmatics and non-asthmatics within WTC Health Program participants

	Any Job Change Asthmatics (n = 704)		Any Job change Non-Asthmatics (n = 6451)	
Variables	**Coeff**	**95% CI**	**Coeff**	**95% CI**
Male	REF		REF	
Female	1.15	(.91-1.45)	1.15	(1.04-1.28)*
Race/ethnicity				
Non-Hispanic White	REF		REF	
Hispanic	0.88	(.62-1.25)	0.81	(.72-.91)*
Non-Hispanic Black	0.17	(.03-1.09)	0.94	(.70-1.27)
Asian	1.18	(.72-1.95)	0.8	(.63-1.02)
Other	0.94	(75-1.19)	0.98	(.90-1.07)
Education categories				
Less than high school	REF		REF	
High school or equivalent	0.85	(.69-1.06)	0.81	(.75-.88)*
More than high school	1.3	(.88-1.92)	1.02	(.83-1.25)
Income categories				
<$30,000	REF		REF	
$30-60,000	0.87	(.56-1.34)	0.66	(58-.76)*
$60-80,000	0.91	(.56-1.45)	0.71	(.62-.82)*
>$80,000	1.09	(.70-1.70)	0.71	(61-.82)*
Age categories				
18-29	REF		REF	
30-39	0.72	(.44-1.17)	1.04	(.85-1.28)
40-49	1.03	(.65-1.64)	1.3	(1.07-1.59)*
50-59	1.21	(.75-1.96)	1.73	(1.41-2.13)*
60 and above	0.97	(.72-1.30)	2.36	(1.88-2.96)*
Occupational categories				
Protective service	REF		REF	
Construction	0.75	(.51-1.10)	1.2	(1.09-1.33)*

Utility	0.65	(.43-1.00)	0.82	(.70-.96)*
Transportation	1.16	(.72-1.87)	1.06	(.91-1.24)
Business	1.1	(.67-1.80)	0.85	(.70-1.03)
Other	0.97	(.72-1.30)	1.05	(.95-1.17)
WTC arrival time				
On 9/11 in dust cloud	REF		REF	
On 9/11 not in dust cloud	0.98	(.77-1.25)	0.97	(.88-1.07)
Arrived 9/12 or later	0.91	(.71-1.16)	0.93	(.84-1.01)
Missing	1.17	(.85-1.60)	1.01	(.90-1.13)
Respiratory protection equipment use				
Did not wear one	1.13	(.88-1.46)	0.95	(.87-1.04)
Nuisance dust/surgical/disposal	1.41	(1.04-1.91)*	1.05	(.95-1.17)
Half-face or full respirator	1.65	(.84-3.22)	1.31	(.73-2.35)
Location of work in Sept 2001				
Adjacent to pile	0.98	(.79-1.20)	0.93	(.86-.99)*
Landfill	1.19	(.69-2.04)	1.09	(.89-1.34)
Barges/loading piers	1.33	(.64-2.76)	1.18	(.90-1.54)
OCME	0.62	(.23-1.63)	0.95	(.70-1.28)
Elsewhere South of Canal St	0.93	(.62-1.38)	0.94	(.81-1.08)
Missing	1.03	(.61-1.74)	0.88	(.72-1.08)
Total hours on site Sept 2001	1	(.99-1.00)	1	(1.00-1.00)*

*p<.05

Appendix 6.

Increased Rates of Asthma among World Trade Center Disaster Responders

Increased Rates of Asthma Among World Trade Center Disaster Responders

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Background *Studies have documented high rates of asthma symptoms among responders to the World Trade Center (WTC) disaster. However, whether there are increased rates of asthma among responders compared to the general population is unknown.*
Methods *The study population consisted of a prospective cohort of 20,834 responders participating in the WTC Medical Monitoring and Treatment Program between July 2002 and December 2007. We calculated prevalence and standardized morbidity ratios (SMRs) of lifetime asthma and 12-month asthma (defined as $\geq$1 attacks in the prior 12 months) among WTC responders. The comparison population consisted of >200,000 adults who completed the National Health Interview Survey in 2000 (for pre-9/11 comparisons) and between 2002 and 2007 (for post-9/11 comparisons).*
Results *WTC responders were on average 43 $\pm$ 9 years old, 86% male, 59% white, and 42% had an occupation in protective services. The lifetime prevalence of asthma in the general population was relatively constant at about 10% from 2000 to 2007. However, among WTC responders, lifetime prevalence increased from 3% in 2000, to 13% in 2002, and 19% in 2007. The age-adjusted overall SMR for lifetime asthma among WTC responders was 1.8 (95% CI: 1.8–1.9) for men and 2.0 (95% CI: 1.9–2.1) for women. Twelve-month asthma was also more frequent among WTC responders compared to the general population (SMR 2.4, 95% CI: 2.2–2.5) for men and 2.2 (95% CI: 2.0–2.5) for women.*
Conclusions *WTC responders are at an increased risk of asthma as measured by lifetime prevalence or active disease.* Am. J. Ind. Med. 55:44–53, 2012.

KEY WORDS: World Trade Center responders; asthma; NHIS

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INTRODUCTION

The collapse of the World Trade Center (WTC) towers on September 11, 2001 and associated fires killed about 3,000 people and exposed a large number of responders and nearby residents to the potential toxic effect of multiple airborne pollutants.

Multiple health problems related to exposures to the WTC disaster have been documented in the literature [Clark et al., 2001; Wheeler et al., 2007; CDC, 2002; Prezant et al., 2002; Banauch et al., 2003, 2005; McGee et al., 2003; Feldman et al., 2004; Landrigan et al., 2004; Skloot et al., 2004; Herbert et al., 2006; Farfel et al., 2008; Prezant, 2008; Brackbill et al., 2009; Aldrich et al., 2010; Weiden et al., 2010]. In particular, several studies have described a high prevalence of pulmonary conditions such as abnormal pulmonary function tests (low forced expiratory volume in 1 s and forced vital capacity), airway hyperreactivity, respiratory symptoms of cough, wheezing, and dyspnea, as well as diagnoses such as asthma and reactive airways dysfunction syndrome [Wheeler et al., 2007; CDC, 2002; Prezant et al., 2002; Banauch et al., 2003, 2005; Feldman et al., 2004; Landrigan et al., 2004; Skloot et al., 2004; Herbert et al., 2006; Farfel et al., 2008; Prezant, 2008; Brackbill et al., 2009; Aldrich et al., 2010; Weiden et al., 2010]. Moreover, a recent study showed that exposed firefighters had a large decline in FEV_1 that persisted up to 6 years following the WTC disaster [Aldrich et al., 2010]. These data suggest an increased rate of pulmonary disorders (in particular asthma) among WTC responders. However, there are no studies comparing rates of asthma in a cohort of WTC responders to those found in the general United States (US) population.

In this study, we used data from the National Health Interview Survey (NHIS), a probability sample of the US population, to assess whether WTC responders have an increase of burden of asthma compared to the general population and to describe temporal trends in the prevalence of asthma among WTC responders.

METHODS

The study cohort consisted of WTC responders who participated in the WTC Medical Monitoring and Treatment Program (MMTP) between July 16, 2002 and December 31, 2007, and consented to have their information used for research purposes. Participants underwent a comprehensive baseline interview and then were followed every 12–18 months with periodic exams. Follow-up rates in the MMTP were 71% and 42% for the first and second follow-up visits, respectively. Details regarding eligibility criteria have been published elsewhere [Herbert et al., 2006]. The NHIS, a stratified multistage probability cluster sample of US households, was used to obtain expected rates of asthma in the general US population [Pleis and Barnes, 2008]. We used NHIS data from the year 2000 to obtain data regarding pre-9/11 asthma rates and from years 2002 to 2007 to estimated asthma rates in subsequent years. NHIS has a cross-sectional design with a different sample of responders sampled in each wave. Both the WTC questionnaire and the NHIS are interviewer-administered and collect self-reports of symptoms and illnesses. The study was approved by the Mount Sinai School of Medicine's Institutional Review Board.

The items used in the WTC and NHIS survey to ascertain lifetime history of asthma or presence of 12-month asthma symptoms are shown in Table I. Briefly, both

TABLE I. Case Definitions of Lifetime Asthma and 12-Month Asthma in the National Health Interview Survey and World Trade Center Medical Monitoring and Treatment Program

Outcome	NHIS	WTC
Lifetime asthma	Have you ever been told by doctor or other health professional that you had asthma?	Has a doctor ever diagnosed you with asthma, cough variant asthma, or reactive airways dysfunction syndrome?
12-month asthma	During the past 12 months, have you had an episode of asthma or an asthma attack?	When was your last attack? (If yes to above question)
Converting WTC information to the NHIS 12-month asthma definition	Month and year of the last asthma attack collected from responders were used to match with NHIS 12-month asthma episodes definition by restricting a positive response within 12 months prior to the initial monitoring program visit. For example, if the last asthma attack was in 01/1999 and the baseline (initial) monitoring visit was 01/2004 then the responder was classified as not having active. Conversely, if the last asthma attack was in 01/2003 and the baseline (initial) monitoring visit was 01/2004 then the individual was classified as having 12-month asthma	
Calculating pre-9/11 (year 2000) prevalence of lifetime and 12-month asthma	Month and year of the last asthma attack was used to calculate lifetime prevalence by restricting a positive response before 01/2001 among responders reported "Yes" to the question "Has a doctor ever diagnosed you with asthma, cough-variant asthma, or reactive airways dysfunction syndrome (RADS)?" 12-month prevalence was calculated by limiting the last attack date between 01/2000 and 12/2000 among who reported a positive answer to the lifetime asthma	

surveys asked participants if they were ever diagnosed by a doctor as having asthma (the WTC survey also included history of reactive airways dysfunction syndrome). This information was used to determine the lifetime prevalence of asthma. Lifetime prevalence included baseline and follow-up visits data. Twelve-month asthma was ascertained based on responses to different questions in the NHIS and WTC program. As part of NHIS, participants reported whether they had an asthma attack during the prior 12 months. WTC responders reported the date of their last asthma attack only as part of the baseline questionnaire and this information was used, in combination with the date of the interview, to determine if the participant had an attack in the prior 12 months.

Age was grouped into the following categories: 18–29, 30–39, 40–49, 50–59, and >60 years of age. In the WTC sample, race and ethnicity were categorized based on the Office of Management and Budget classification [Durch and Madans, 1997]. However, in the NHIS, ''Native Hawaiian/other Pacific Islander'' and ''American Indian/Alaskan Native'' were coded in the in the ''other race'' category. Thus, this categorization was also applied to the WTC data. Both WTC and NHIS occupation were coded according to the 2000 Standard Occupational Classification (SOC) developed by the Bureau of Labor Statistics [2009]. Smoking status was categorized into current, former, and never smokers.

Statistical Analyses

The χ^2-test was used to compare the distribution of baseline characteristics of NHIS and WTC participants. Crude annual prevalence of lifetime and 12-month asthma were calculated using NHIS sample weighting methods [NCHS, 2008]. Age-adjusted standardized morbidity ratios (SMRs), the ratio of observed to expected counts, were calculated with a 95% confidence interval (CI) based on the Poisson distribution [Sahai and Khurshid, 1993]. Age-, gender-, and occupation-specific SMRs were calculated using an indirect standardization method to determine expected counts from NHIS [Checkoway et al., 2004]. Analyses were performed with Stata 11.0 (Stata Corp., College Station, TX) and SAS 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

Overall 20,843 WTC responders were included in the study cohort. Mean age of WTC responders was 43 (±9 years). Eight-six percent were males, 59% White, 11% Black, and 24% of Hispanic ethnicity. The most common occupations were protective services (42%) and construction (25%). Compared to NHIS participants, WTC responders were more likely to be between 30 and 49 years of age, male, non-White, and of Hispanic ethnicity ($P \leq 0.001$ for all comparisons Table II).

Prevalence of Lifetime Asthma and 12-Month Asthma

Lifetime asthma prevalence between 2002 and 2007 in NHIS remained relatively stable (10.7%, 10.7%, and 10.9% in 2002, 2005, and 2007, respectively; Table III). Conversely, among WTC responders, the prevalence increased from 2.9% pre-9/11 (95% CI: 2.7–3.2%) to 12.8% in 2002 (95% CI: 11.5–14.1%) and 19.4% in 2007 (95% CI: 18.4–20.4%). Compared to pre-9/11, lifetime prevalence of asthma increased more than sixfold in 2007 among WTC responders (Fig. 1). These patterns were consistent across different age, race, gender, occupational group, and smoking status groups.

The average prevalence of 12-month asthma (≥1 attack in the prior 12 months) was 3.7% in NHIS and 6.3% in WTC, for the period 2002–2007. Rates of 12-month asthma prevalence remained stable in the NHIS population (3.8%, 3.9%, and 3.8%, for years 2002, 2005, and 2007, respectively; Table IV). However, there were large increases in 12-month asthma rates among WTC responders, from 0.2% (95% CI: 0.1–0.2%) in 2000 to 8.2% (95% CI: 6.8–9.8%) in 2005, and, a slight decrease between 2005 and 2007 (7.8%; 95% CI: 6.9–8.7% for the latter). Compared to the year 2000 (pre-9/11), 12-month asthma increased about 40-fold among WTC responders (Fig. 1).

Standardized Morbidity Ratios

The age-adjusted overall SMR for lifetime asthma prevalence (1.6, 95% CI: 1.6–1.7) was elevated among WTC responders in all years following 9/11. The age-adjusted overall SMR (1.7, 95% CI: 1.6–1.8) for 12-month asthma among WTC responders was also elevated during the 2002–2005 period and did not change thereafter. Both lifetime and 12-month asthma prevalence were considerably lower in 2000 among these WTC responders than among the NHIS participants (SMR: 0.3, 95% CI: 0.3–0.4 and 0.03, 95% CI: 0.02–0.04, respectively; Fig. 2).

Gender- and age-specific lifetime and 12-month asthma SMRs increased over time for both WTC women and men (Table V). Overall lifetime asthma SMRs were elevated in all age groups, ranging from 1.2 (95% CI: 1.1–1.3) in the 18- to 29-year-old group to 1.7 (95% CI: 1.7–1.8) in the 40- to 49-year-old group. Similarly, age-stratified 12-month asthma SMRs were increased in all groups from 1.4 (95% CI: 1.2–1.6) in 50- to 59-year-old group to 1.7 (95% CI: 1.6–1.9) in the 40- to 49-year-old group.

Occupation-specific lifetime asthma SMRs were also elevated among all groups; SMRs ranged from 1.5 (95% CI: 1.5–1.6) in protective service workers to 2.0 (95% CI:

TABLE II. Characteristics of National Health Interview Survey Population and World Trade Center Responders (Baseline Visit)

	Year													
	2000		2002		2003		2004		2005		2006		2007	
Variable	**NHIS**	**WTC**	**NHIS**	**WTC**	**NHIS**	**WTC**	**NHIS**	**WTC**	**NHIS**	**WTC**	**NHIS**	**WTC**	**NHIS**	**WTC**
Total, N	32,374	20,843[a]	31,044	2,970	30,852	5,755	31,326	3,267	31,428	1,478	24,275	3,466	23,393	3,907
Age, years (%)														
18–29	22.0	5.6	21.8	7.2	21.6	7.0	21.7	6.6	21.8	4.9	21.8	4.3	22.1	3.2
30–39	20.7	34.2	19.7	36.0	19.5	34.5	19.1	37.1	18.6	34.4	18.2	34.2	17.9	29.8
40–49	21.0	39.4	21.3	35.6	20.9	38.0	20.6	39.6	20.4	41.7	20.4	40.5	19.9	42.0
50–59	14.9	16.6	15.8	17.9	16.3	16.4	16.3	13.5	16.9	15.2	17.3	16.9	17.0	18.9
$\geq$60	21.5	4.2	21.4	3.4	21.8	4.2	22.3	3.2	22.2	3.8	22.2	4.0	23.1	6.2
Gender (%)														
Female	52.1	14.3	52.0	11.8	52.0	13.7	51.9	13.1	51.8	15.4	51.8	16.8	51.7	15.6
Male	47.9	85.7	48.0	88.2	48.0	86.3	48.1	86.9	48.2	84.6	48.2	83.2	48.3	84.4
Race (%)														
White	81.2	59.2	80.8	62.0	83.5	56.9	83.0	60.0	82.9	58.6	81.5	58.2	81.0	61.3
Black	11.3	10.7	11.4	12.0	11.3	8.3	11.4	11.3	11.4	13.0	11.9	10.2	11.8	12.6
Asian	3.3	1.3	3.5	1.7	3.5	1.1	3.7	0.9	3.7	1.6	4.6	1.5	4.7	1.7
Other	4.3	28.3	4.2	24.4	1.8	33.8	1.9	27.9	2.0	26.9	2.1	30.2	2.5	24.4
Ethnicity (%)														
Hispanic	10.5	24.2	11.0	19.4	12.3	25.0	12.5	24.3	12.8	23.9	13.0	28.3	13.4	23.2
Non-Hispanic	89.5	57.1	89.0	66.9	87.7	55.7	87.6	56.5	87.3	63.3	87.0	52.2	86.6	54.5
Occupation (%)[b]														
Protective service	1.2	41.5	1.2	23.9	1.3	30.9	1.7	47.5	1.6	47.3	1.7	53.4	1.8	52.9
Construction and extraction	3.3	25.4	3.6	25.1	3.7	35.5	5.2	28.9	5.6	25.8	5.5	17.3	5.1	14.9
Installation, maintenance, and repair	2.2	7.2	2.3	19.5	2.4	5.8	3.4	4.0	3.0	4.9	3.3	3.8	3.3	6.4
Transportation and material moving	4.7	4.3	4.5	4.8	4.6	5.7	5.6	3.6	5.5	3.0	5.4	3.9	5.2	3.3
Other	52.4	16.9	51.0	19.1	49.3	17.1	74.0	13.3	74.4	15.5	73.3	17.4	74.8	18.0
Smoking (%)														
Current smoker	23.1	16.2	22.3	18.6	21.3	18.2	20.7	17.6	20.7	17.3	20.6	12.7	19.5	12.8
Former smoker	22.0	23.9	22.4	24.0	21.6	26.2	21.2	22.4	21.4	24.2	20.8	22.9	21.2	22.7
Never smoker	54.1	58.3	54.3	54.4	55.9	54.2	57.1	58.8	57.1	57.1	57.4	63.3	57.8	62.9

Unweighted number of participants in the National Health Interview Survey; all *P*-values for comparisons between the National Health Interview Survey participants and World Trade Center responders were $<$0.001; rates for the year 2001 were omitted given that exposure among World Trade Center responders occurred in September that year.
[a]Total number of World Trade Center responder population.
[b]Classified based on the 1990 Standard Occupational Classification for years 2000–2004 and the 2000 Standard Occupational Classification by Bureau of Labor Statistics for years 2005–2007.

1.8–2.2) in installation, maintenance, and repair workers. Similarly, specific acute asthma SMRs were elevated in all occupation groups, ranging from 1.6 (95% CI: 1.2–2.2) in transportation and material moving workers to 2.3 (95% CI: 1.9–2.8) in installation, maintenance, and repair workers (Table VI).

DISCUSSION

Exposure to airborne pollutants following the collapse of the WTC towers and during the recovery efforts has been linked to acute reductions in lung function, increased pulmonary symptoms, and high frequency of asthma among responders. In this study, we showed that rates of self-reported lifetime asthma and 12-month asthma were significantly increased among a large sample of WTC responders, when compared to the general US population. Most of the increased risk became evident in the early years after 9/11 and has remained elevated but relatively stable since 2005. Further studies are necessary to identify risk factors for developing asthma in this population. Appropriate planning will be important to reduce the risk of exposure-related asthma in future natural or unnatural disasters.

A study conducted using the WTC Health Registry (a large cohort of rescue and recovery workers and residents

TABLE III. Lifetime Asthma Prevalence Among World Trade Center Responders (Included Baseline and Follow-Up Visits) and National Health Interview Survey Population

	Year													
	2000		2002		2003		2004		2005		2006		2007	
Variable	NHIS 32,374	WTC 20,843[a]	NHIS 31,044	WTC 2,970	NHIS 30,852	WTC 5,755	NHIS 31,326	WTC 3,740	NHIS 31,428	WTC 4,797	NHIS 24,275	WTC 6,043	NHIS 23,393	WTC 7,620
Total (%)	9.3	2.9	10.7	12.8	9.7	11.9	9.9	14.3	10.7	17.5	11.0	17.7	10.9	19.4
Age, years (%)														
18–29	11.9	4.6	13.5	12.2	11.5	10.0	11.1	14.6	12.7	17.9	13.3	16.8	14.0	20.3
30–39	8.2	3.1	10.0	14.0	9.0	12.4	8.7	14.6	10.1	16.5	10.2	17.5	9.9	19.6
40–49	8.7	2.9	10.5	12.9	9.6	12.8	9.5	14.7	10.1	18.5	9.6	18.6	10.0	20.4
50–59	8.9	2.5	10.8	10.2	9.8	10.6	10.0	13.1	10.5	16.3	10.8	16.7	9.5	18.1
≥60	8.5	1.8	8.5	14.0	8.6	7.9	10.0	12.2	10.1	19.9	10.9	14.5	10.6	14.7
Gender (%)														
Female	10.5	2.8	11.9	21.1	11.2	15.5	11.2	23.5	12.6	24.7	12.4	23.2	12.2	28.6
Male	8.0	3.0	9.3	11.7	8.1	11.3	8.5	13.0	8.7	16.3	9.5	16.7	9.6	17.9
Race (%)														
White only	9.3	2.6	10.5	12.4	9.6	12.6	9.7	13.9	10.6	18.2	10.9	17.8	11.1	18.3
Black/African American only	9.2	4.5	12.1	14.3	10.8	13.3	11.2	14.8	11.7	16.8	11.9	20.6	10.2	19.4
Asian only	6.2	1.8	7.9	6.1	5.9	6.6	6.9	15.4	7.7	15.1	8.3	15.6	8.1	19.0
Other	10.8	3.2	11.5	13.3	14.0	10.6	15.0	14.9	14.7	16.2	18.2	16.7	15.5	22.2
Ethnicity (%)														
Hispanic	7.2	3.7	7.3	15.8	7.3	10.4	7.5	16.1	7.6	17.4	8.2	16.8	9.0	23.2
Non-Hispanic	9.5	2.9	11.1	12.6	10.1	12.6	10.2	13.9	11.2	18.0	11.4	18.4	11.2	19.0
Occupation (%)[b]														
Protective service	9.9	3.5	11.5	14.8	8.4	16.1	8.8	15.5	11.1	20.3	14.0	19.0	16.6	19.7
Construction and extraction	6.7	2.2	7.6	10.2	5.7	7.8	8.1	9.0	7.5	13.5	7.2	13.7	8.8	16.5
Installation, maintenance, and repair	5.4	3.2	8.1	13.6	7.3	13.0	7.4	15.0	7.4	15.6	11.3	20.7	8.5	20.3
Transportation and material moving	6.8	3.1	8.4	11.4	9.2	10.7	9.7	14.8	9.6	17.5	11.7	12.3	9.2	21.2
Other	9.4	2.6	10.6	13.9	9.4	13.4	10.6	20.2	11.5	19.2	11.6	20.2	11.6	22.3
Smoking (%)														
Current smoker	10.2	3.2	12.6	11.8	11.4	10.4	10.8	11.9	12.2	16.1	13.1	14.9	12.7	17.6
Former smoker	10.8	2.8	11.3	12.5	11.2	12.4	12.3	15.6	11.1	18.8	11.9	18.6	12.4	20.5
Never smoker	8.3	3.0	9.7	13.2	8.7	12.2	8.8	14.5	10.1	17.2	10.0	18.0	9.9	19.4

Unweighted number of participants in the National Health Interview Survey; all *P*-values for comparisons between the National Health Interview Survey participants and World Trade Center responders were <0.001; rates for the year 2001 were omitted given that exposure among World Trade Center responders occurred in September that year.
[a]Total number of World Trade Center responder population.
[b]Classified based on the 1990 Standard Occupational Classification for years 2000–2004 and the 2000 Standard Occupational Classification by Bureau of Labor Statistics for years 2005–2007.

in lower Manhattan on 9/11), reported high rates of new onset asthma [Brackbill et al., 2009]. In that study, new onset asthma was as high as 10% among participants with no prior history of asthma 5–6 years after 9/11. Self-reported newly diagnosed asthma was positively associated with higher exposure to the WTC site and decreased with use of a mask or a respirator [Wheeler et al., 2007; Feldman et al., 2004]. Similarly, studies of firefighters found large declines in FEV_1 [Prezant et al., 2002] and high prevalence of obstructive disease among WTC responders [Weiden et al., 2010]. Our study extends these results by showing that the rates of asthma as well as active disease are increased among WTC responders when compared with those expected in the general population, and that this increased risk persists several years after exposure.

Our results suggest that the increased risk of both prevalent and acute asthma is present across the different age, sex, and most occupation categories. Additional studies are necessary to further define the groups and type of

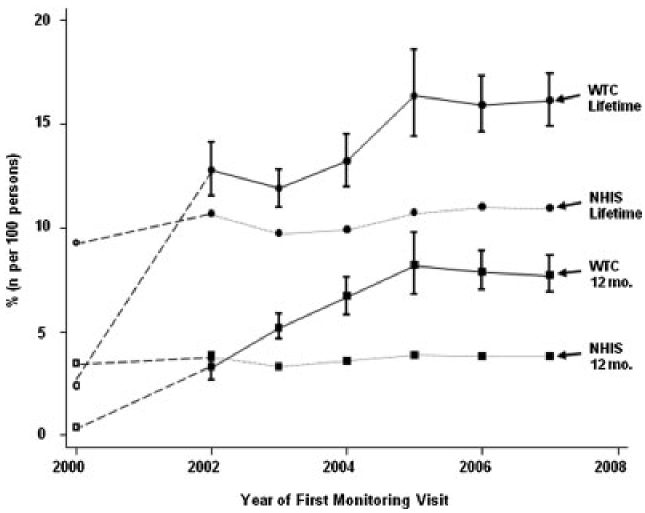

FIGURE 1. Crude prevalence of lifetime and 12-month asthma in the National Health Interview Survey and World Trade Center Medical Monitoring and Treatment Program.

WTC exposures associated with higher risk of new onset asthma. We also found that rates of lifetime and acute asthma were significantly lower among WTC responders than the general population in 2000. This finding is likely due to a healthy worker effect and suggests that our findings of increased rates in subsequent years are probably a conservative estimate of the risk of asthma among WTC responders.

The collapse of the WTC towers generated a complex mixture of airborne pollutants including pulverized building materials and products of combustion [McGee et al., 2003]. Following the initial collapse, structural fires continued for several weeks, releasing products of combustion and pyrolysis. Moreover, the use of gasoline- and diesel-powered machinery that was necessary for the removal of debris in subsequent weeks, contributed additional products of combustion. Many WTC responders were exposed to these pollutants [Clark et al., 2001] with little or no respiratory protection given the difficult working conditions in the first days after the disaster [Feldman et al., 2004]. These exposures likely lead to inflammation of the nasal passages, throat, and lower airways yielding irritant-induced rhinosinusitis, pharyngitis, reactive airways disease syndrome (RADS) [Henneberger et al., 2003], and asthma [Banauch et al., 2003, 2005]. Prior data shows that comparable levels of exposure to airborne pollutants in occupational settings has been associated with development of RADS [Brooks et al., 1985; Lombardo and Balmes, 2000]. Moreover, experimental studies using mice have shown that exposure to high levels of fine particulate matter from the WTC site led to the development of mild-to-moderate pulmonary inflammation and increases in airway hyper-responsiveness [Gavett et al., 2003].

There are several strengths and limitations of this study. Our study population consisted of a large cohort of WTC responders representing many different types of workers who participated in the WTC rescue and recovery effort. The comparison group was drawn from the NHIS, a probability sample of the entire US population. Thus, the generalizability of our findings should be strong. Although another population based survey, the Behavioral Risk Factor Surveillance System (BRFSS), showed about a 4% higher lifetime asthma prevalence in New York State (10.7% in 2000, 11.1% in 2001, 11.5% in 2002, 11.7% in 2003, 14.2% in 2004, 13.8% in 2005, 13.1% in 2006, and 14.0% in 2007) than the NHIS (US total prevalence), the rate was still lower than among responders. Although there was a smaller difference of lifetime asthma prevalence with the BRFSS data, what would remain is the increased trend in asthma among responders that occurred over time after September 11, as compared to the BRFSS asthma trend at the same period. The BRFSS measures current asthma prevalence rather than a 12-month asthma attack or episode, which we measured in this study. Thus, only lifetime asthma prevalence was comparable. Asthma prevalence was ascertained by self-report, which might be subject to reporting bias. However, both the WTC program and the NHIS collected self-reported diagnosis of asthma and presence of acute asthma episodes were evaluated using similar items. Thus, reporting bias, if present, should be comparable in both groups and therefore unlikely to explain our results. WTC responders in the MMTP undergo periodic health exams and are referred for medical evaluation if abnormalities are identified. This greater contact with healthcare providers may increase the probability that WTC responders are diagnosed more often with asthma when compared to the general population, a factor that may partially explain our findings. Increased rates of self-reported asthma among WTC responders may be also due to selection bias. Responders with asthma or other health problems are probably more likely to enroll in the MMTP and return for the follow-up exams. However, in the baseline visits SMR trends by visit year showed that individuals who enrolled in the early years of the program also had an increased risk for lifetime and 12-month asthma. Moreover, asthma rates in the New York City Fire Department's MMTP, a prospective cohort of all firefighters exposed to the WTC site, were similar to those observed in our population [Prezant et al., 2002; Banauch et al., 2003; Prezant, 2008].

Another potential limitation is related to differences in the wording of items assessing asthma prevalence in the WTC questionnaire and the NIHS (Table I). Twelve-month asthma in particular, was estimated among WTC responders by combining information from different questions, a factor that might affect comparability across studies. However, 23% of the WTC responders diagnosed with asthma

TABLE IV. Prevalence of 12-Month Asthma Among World Trade Center Responders (Baseline Visit Only) and National Health Interview Survey Population

	Year													
	2000		2002		2003		2004		2005		2006		2007	
Variable	NHIS 32,374	WTC 20,843[a]	NHIS 31,044	WTC 2,970	NHIS 30,852	WTC 5,755	NHIS 31,326	WTC 3,267	NHIS 31,428	WTC 1,478	NHIS 24,275	WTC 3,466	NHIS 23,393	WTC 3,907
Total (%)	3.5	0.2	3.8	3.3	3.3	5.2	3.6	6.7	3.9	8.2	3.8	7.9	3.8	7.8
Age, years (%)														
18–29	3.8	0.2	4.2	3.7	3.5	3.3	3.5	4.2	3.9	11.0	3.6	9.3	4.0	10.6
30–39	3.2	0.2	3.8	3.9	3.3	5.4	3.3	6.6	4.0	7.9	3.9	7.9	3.7	7.3
40–49	3.8	0.2	4.0	3.5	3.6	5.8	3.7	7.6	4.3	8.3	4.0	8.1	4.2	8.2
50–59	3.4	0.1	3.8	1.7	3.8	5.0	4.1	5.9	3.9	7.6	4.7	7.5	3.6	6.9
≥60	3.0	0.2	3.0	1.0	2.6	2.9	3.4	4.8	3.3	8.9	3.2	5.7	3.5	7.9
Gender (%)														
Female	4.6	0.2	5.0	7.1	4.5	8.9	4.5	12.6	5.2	14.5	5.1	11.5	5.0	14.6
Male	2.2	0.2	2.4	2.8	2.1	4.7	2.6	5.8	2.5	7.0	2.4	7.2	2.6	6.5
Race (%)														
White	3.5	0.2	3.7	3.4	3.3	5.6	3.5	6.9	3.9	7.9	3.8	7.9	3.8	7.0
Black	3.3	0.3	4.3	3.4	3.8	5.7	4.3	6.2	3.8	10.4	3.6	9.9	3.9	8.1
Asian	1.8	0.0	2.5	0.0	1.1	4.9	1.7	0.0	2.8	8.7	2.4	7.7	2.4	10.5
Other	4.2	0.2	4.5	3.0	5.2	4.5	5.2	6.6	6.9	7.8	7.5	7.3	5.1	9.2
Ethnicity (%)														
Hispanic	2.8	0.1	2.3	3.8	2.7	4.2	2.5	6.4	2.9	8.8	2.9	7.7	3.2	10.0
Non-Hispanic	3.5	0.2	3.9	3.1	3.4	5.6	3.7	6.1	4.0	7.9	3.9	8.6	3.9	7.3
Occupation (%)[b]														
Protective service	2.7	0.2	3.3	4.2	3.1	7.5	2.5	7.7	3.8	9.3	4.6	8.1	5.6	7.3
Construction and extraction	1.7	0.1	1.2	2.0	1.5	3.0	2.6	3.5	2.0	4.5	2.4	5.3	2.3	5.0
Installation, maintenance, and repair	1.6	0.3	2.1	3.6	1.9	5.1	1.9	6.2	2.9	12.5	3.3	10.6	3.3	8.5
Transportation and material moving	2.0	0.2	1.9	0.7	1.8	3.4	3.6	9.5	3.0	6.7	3.8	5.2	3.5	8.5
Other	3.4	0.2	3.8	4.2	3.3	6.7	3.9	9.7	4.1	9.2	4.0	9.9	4.1	11.3
Smoking (%)														
Current smoker	3.7	0.2	4.7	2.4	4.1	4.4	4.2	4.2	4.4	6.3	4.7	5.9	4.2	6.4
Former smoker	3.9	0.1	3.9	3.6	3.9	5.3	4.4	8.2	4.0	10.3	4.1	8.4	4.3	8.1
Never smoker	3.2	0.2	3.3	3.5	2.9	5.5	3.1	6.8	3.6	8.1	3.4	8.1	3.5	8.0

Unweighted number of participants in the National Health Interview Survey; all *P*-values for comparisons between the National Health Interview Survey participants and World Trade Center responders were <0.001; rates for the year 2001 were omitted given that exposure among World Trade Center responders occurred in September that year.
[a]Total number of World Trade Center responder population.
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did not provide the date of their last asthma attack. These individuals were classified as not having 12-month asthma and thus, contributed only to the denominator when estimating 12-month asthma rates, likely making our results conservative.

Also we did not survey WTC workers before 9/11/01, so recall bias may have affected their reports of asthma in the year 2000 and earlier years. To check this recall bias, the percentage of those reporting lifetime or 12-month asthma attack by year of monitoring visit were checked and there was no significant difference between years (2002–2007). This means that it is less likely for a recall bias to play a role on such a low prevalence. In contrast with recall bias, there may be a healthy worker effect which means WTC responders and volunteers were much healthier than the general population, which may be a better explanation of such a low prevalence of lifetime asthma and episodes prior to 9/11. To control this healthy worker effect, we matched occupations between WTC and NHIS, but a still lower prevalence in WTC responders was observed within the same occupational group in 2000. This may imply that WTC responders were even healthier than other workers in the same occupational group. Race and ethnicity are also known risk factors of asthma, but these are not adjusted in this study, because we found no relationships between these factors and asthma among

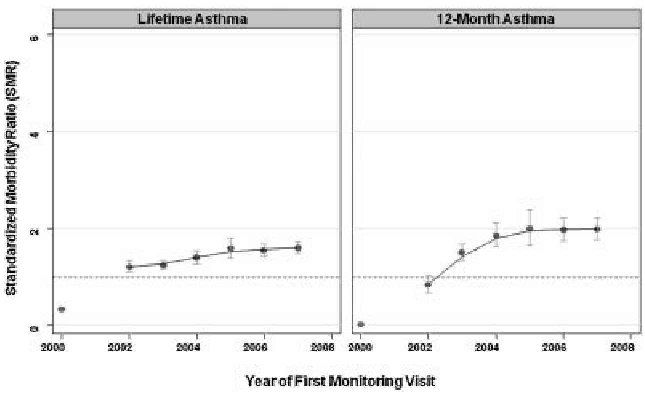

FIGURE 2. Age-adjusted standardized morbidity ratios for lifetime and 12-month asthma among World Trade Center responders compared to National Health Interview participants.

responders. However, other socioeconomic factors such as income level or household size should be investigated, but unfortunately no data has been collected to capture this information.

In summary, this study shows that WTC responders have increased rates of asthma as well as active disease when compared to the general US population. These results suggest that medical surveillance and treatment programs should be established following similar exposures in the future. Similarly, objective measures of lung function and airway responsiveness should be obtained in exposed WTC responders with respiratory symptoms. Early diagnosis and long-term monitoring are necessary to avoid irreversible lung changes among WTC responders with asthma. Further research is also needed to clarify the physiopathology of exposure-related asthma as well as to develop plans to decrease the risk of pulmonary disease among future responders to similar disasters.

TABLE V. Age and Sex Stratified Standardized Morbidity Ratio of Lifetime and 12-Month Asthma

	2000		2002		2003		2004		2005		2006		2007	
Age by gender	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**
Lifetime asthma														
Male	0.4	0.4–0.5	1.3	1.2–1.5	1.5	1.4–1.6	1.7	1.5–1.8	2.0	1.9–2.2	1.9	1.8–2.1	2.1	2.0–2.3
18–29	0.4	0.3–0.6	0.8	0.5–1.2	0.9	0.6–1.3	1.3	0.9–1.9	1.4	1.0–2.0	1.3	0.9–1.8	1.3	1.0–1.7
30–39	0.4	0.4–0.5	1.6	1.3–1.9	1.5	1.3–1.7	1.8	1.5–2.1	2.0	1.7–2.3	2.1	1.8–2.3	2.4	2.2–2.7
40–49	0.5	0.4–0.5	1.4	1.2–1.7	1.6	1.4–1.8	1.7	1.4–2.0	2.3	2.0–2.5	2.1	1.9–2.3	2.1	1.9–2.3
50–59	0.3	0.3–0.4	1.0	0.8–1.4	1.5	1.3–2.0	1.6	1.2–2.0	1.9	1.6–2.3	1.7	1.4–2.0	2.2	1.9–2.5
≥60	0.2	0.1–0.4	1.8	0.9–3.2	1.0	0.6–1.7	1.2	0.7–2.1	2.0	1.3–2.8	1.3	0.8–1.9	1.6	1.2–2.1
Female	0.3	0.2–0.3	1.7	1.4–2.2	1.4	1.1–1.6	2.1	1.8–2.6	2.0	1.7–2.3	2.0	1.7–2.2	2.4	2.2–2.7
18–29	0.3	0.1–0.6	1.7	0.7–3.3	0.9	0.4–1.7	1.5	0.6–3.1	1.7	0.9–3.1	1.4	0.8–2.3	2.1	1.2–3.5
30–39	0.3	0.2–0.4	1.9	1.3–2.8	1.5	1.1–2.0	2.4	1.7–3.3	1.7	1.2–2.3	1.8	1.4–2.3	2.3	1.9–2.8
40–49	0.2	0.2–0.3	1.7	1.1–2.4	1.5	1.2–2.0	2.2	1.6–2.9	2.1	1.6–2.6	2.2	1.8–2.7	2.8	2.4–3.3
50–59	0.3	0.2–0.5	1.4	0.7–2.6	0.9	0.5–1.6	1.9	1.0–3.1	1.8	1.2–2.7	1.9	1.4–2.7	2.1	1.5–2.8
≥60	0.4	0.1–1.0	2.8	0.6–8.3	1.6	0.5–3.8	2.3	0.5–6.6	3.6	2.0–6.1	3.0	1.3–5.9	1.9	1.0–3.2
12-month asthma														
Male	0.1	0.1–0.1	1.2	0.9–1.5	2.4	2.1–2.7	2.5	2.1–2.9	2.6	2.1–3.3	2.1	0.8–4.6	2.5	2.2–2.9
18–29	0.1	0.0–0.3	0.6	0.1–1.7	1.1	0.5–2.1	1.1	0.4–2.3	1.5	0.2–5.5	4.1	1.9–7.8	3.6	1.8–6.4
30–39	0.1	0.0–0.1	1.4	1.0–2.0	2.4	1.9–3.0	2.7	2.1–3.5	2.7	1.8–3.7	3.3	2.6–4.1	3.3	2.5–4.2
40–49	0.1	0.1–0.2	1.5	1.0–2.1	2.6	2.1–3.2	2.8	2.2–3.6	2.8	2.0–3.9	2.5	2.0–3.2	2.1	1.7–2.5
50–59	0.1	0.0–0.2	0.7	0.3–1.4	2.5	1.8–3.5	1.8	1.1–2.9	2.2	1.1–4.1	2.9	2.3–3.6	2.9	2.0–4.1
≥60	0.1	0.0–0.4	0.6	0.0–3.1	1.5	0.5–3.4	2.0	0.6–4.6	3.1	0.6–9.0	2.2	1.5–3.1	2.3	1.2–4.0
Female	0.0	0.1–0.1	1.3	0.9–2.0	1.8	1.4–2.3	2.7	2.0–3.5	2.7	1.8–3.7	2.1	1.6–2.7	2.8	2.3–3.5
18–29	—	—	2.6	0.9–6.1	0.9	0.2–2.7	2.1	0.4–6.1	6.9	2.5–15.0	2.3	0.7–5.3	2.0	0.2–7.3
30–39	0.1	0.0–0.3	1.6	0.8–3.0	1.9	1.2–2.9	2.8	1.7–4.3	2.0	0.8–4.1	1.9	1.2–3.0	2.3	1.4–3.4
40–49	0.0	0.0–0.1	1.2	0.6–2.3	2.2	1.5–3.0	2.7	1.8–4.1	2.0	1.0–3.5	2.4	1.6–3.4	3.2	2.3–4.3
50–59	—[a]	—	0.4	0.0–1.9	1.2	0.5–2.5	2.7	1.2–5.3	3.7	1.5–7.5	1.8	0.9–3.2	2.9	1.7–4.5
≥60	—	—	—	—	1.9	0.2–7.0	—	—	4.0	0.5–14.5	2.9	0.4–10.5	4.1	1.5–9.0

CI, confidence interval; SMR, standardized morbidity ratio.
[a]Not reported given low number of observations.

TABLE VI. Standardized Morbidity Ratio for Lifetime and 12-Month Asthma by Gender and Occupation

	2000		2002		2003		2004		2005		2006		2007	
Occupation by gender	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**	**SMR**	**95% CI**
Lifetime asthma														
Male	0.4	0.4–0.5	1.3	1.2–1.5	1.5	1.4–1.6	1.7	1.5–1.8	2.0	1.9–2.2	1.9	1.8–2.1	2.4	2.2–2.7
Protective service	0.3	0.3–0.4	1.2	0.9–1.5	2.4	2.1–2.7	2.0	0.1–2.3	4.7	0.3–5.3	2.4	0.1–2.6	2.0	0.1–2.2
Construction and extraction	0.3	0.3–0.4	1.4	1.1–1.8	1.5	1.2–1.7	1.2	0.1–1.5	6.6	0.5–7.6	4.8	0.4–5.6	4.9	0.3–5.5
Installation, maintenance, and repair	0.6	0.5–0.8	1.6	1.3–2.1	1.9	1.4–2.6	4.1	0.7–5.8	1.6	0.6–3.1	4.0	0.5–5.2	6.0	0.6–7.3
Transportation and material moving	0.5	0.3–0.7	1.1	0.6–1.9	1.2	0.8–1.6	1.7	0.4–2.8	8.4	1.5–12.0	1.8	0.4–2.6	6.5	0.9–8.5
Other	0.3	0.3–0.4	1.4	1.1–1.8	1.4	1.1–1.8	2.3	0.3–2.9	7.1	0.7–8.7	3.0	0.3–3.6	3.6	0.3–4.1
Female	0.3	0.2–0.3	1.7	1.4–2.2	1.4	1.1–1.6	2.1	1.8–2.6	2.0	1.7–2.3	2.0	1.7–2.2	2.4	2.2–2.7
Protective service	0.6	0.4–0.8	2.0	1.3–2.9	1.6	1.2–2.1	1.8	0.2–2.3	3.6	0.5–4.7	1.4	0.2–1.7	1.9	0.2–2.2
Construction and extraction	0		0.4	0.1–1.6	0.3	0.1–0.8	1.5	0.7–3.5	5.6	1.5–9.4	2.2	0.6–3.6	10.4	2.3–16.0
Installation, maintenance, and repair	0.5	0.1–1.3	2.1	1.0–4.0	0		1.8	1.1–5.3	29.2	11.0–60.1	5.5	2.7–14.0	5.2	1.7–9.6
Transportation and material moving	0.8	0.1–3.0	6.6	1.8–16.8	2.0	0.2–7.1	2.8	1.6–8.2			6.3	4.4–22.6	6.1	2.0–11.5
Other	0.3	0.2–0.4	1.4	0.9–2.1	1.7	1.3–2.2	3.1	0.5–4.2	6.6	0.8–8.3	3.2	0.3–3.9	4.6	0.4–5.5
12-month asthma														
Male	0.1	0.1–0.1	1.2	0.9–1.5	2.4	2.1–2.7	2.5	2.1–2.9	2.6	2.1–3.3	2.1	0.8–4.6	2.5	2.2–2.9
Protective service	0.1	0.0–0.1	1.4	0.9–2.1	3.5	2.9–4.3	5.4	4.4–6.7	2.5	1.8–3.3	2.9	2.4–3.4	1.8	1.5–2.1
Construction and extraction	0.1	0.0–0.2	1.6	0.9–2.7	2.3	1.8–3.0	1.5	1.0–2.1	2.3	1.3–3.8	2.5	1.7–3.6	2.4	1.5–3.4
Installation, maintenance, and repair	0.2	0.1–0.6	1.8	1.1–2.8	2.9	1.7–4.6	3.5	1.4–7.2	4.0	1.7–7.9	3.5	1.9–5.9	2.8	1.6–4.4
Transportation and material moving	0.1	0.0–0.6	0.4	0.0–2.4	1.7	0.8–3.1	3.4	1.6–6.3	2.8	0.6–8.2	1.8	0.7–3.7	2.9	1.2–5.7
Other	0.1	0.0–0.2	1.5	0.8–2.4	2.4	1.7–3.4	2.6	1.6–4.0	2.7	1.3–5.0	3.2	2.2–4.7	3.4	2.5–4.6
Female	0.0	0.0–0.1	1.3	0.9–2.0	1.8	1.4–2.3	2.7	2.0–3.5	2.7	1.8–3.7	2.1	1.6–2.7	2.8	2.3–3.5
Protective service	0.1	0.0–0.2	1.4	0.6–2.6	2.0	1.3–2.8	2.1	1.4–3.1	2.9	1.7–4.5	0.8	0.6–1.2	1.1	0.8–1.5
Construction and extraction	—	—[a]	—	—	0.5	0.1–1.3	0.7	0.1–2.6	0.7	0.0–3.8	0.6	0.1–1.9	1.5	0.3–4.4
Installation, maintenance, and repair	—	—	1.3	0.3–3.8	—	—	3.1	0.9–17.4	25.0	0.6–139.3	—	—	1.9	0.2–7.0
Transportation and material moving	—	—	—	—	11.1	0.3–61.9	2.0	0.1–10.9	—	—	—	—	4.8	1.0–13.9
Other	0.1	0.0–0.2	1.3	0.6–2.4	2.4	1.7–3.5	4.2	2.5–6.2	2.7	1.4–4.8	2.6	1.8–3.7	3.6	2.6–5.0

CI, confidence interval; SMR, standardized morbidity ratio.
[a]Not reported given low number of observations.

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Appendix 7

Title: Incidence of rheumatoid arthritis among World Trade Center responders

Authors: TBN

INTRODUCTION

Early exposure assessments of the World Trade Center (WTC) Disaster yielded a wide range of hazardous substances for the first responders and community residents (Landrigan 2004). Among these were crystalline silica, glass fibers, asbestos, and other heavy metals. Potential adverse health effects of these exposures include rheumatoid arthritis (RA), given the growing body of epidemiologic evidence suggesting that occupational exposures to crystalline silica increases the risk of this disease (Klockars 1987, Steenland 1992, Parks 1999, Reckner 2000, WHO 2000, Olsson 2004, Stolt 2010, Hoovestol 2011, Jones 2012). There is more limited evidence of an association between asbestos and RA; a recent study reported an elevated odds ratio (3.2 95% Confidence Interval 1.3 to 8.0)) among workers of age 65 or older at the Libby, Montana asbestos mine (Noonan 2006). Although the WTC event was of relatively short duration (September 11, 2001 to July 1, 2002) compared to many occupational cohorts, the intensity of exposure and complexity of the airborne toxic cloud were extreme (Herbert 2006). It is appropriate to investigate the hypothesis that WTC responders experience an increased risk of RA.

The link between RA and WTC dust and respirator use has not been studied, although associations with other autoimmune diseases such as sarcoidosis (Crowley 2011) and multiple myeloma (Moline 2009) have been reported. A recently published case-control study of firefighters and EMS workers enrolled in the FDNY WTC Health Program found that prolonged work at the WTC site was associated with post-9/11 systemic autoimmune diseases, independent of acute exposure (Webber 2015). In this study, we evaluated the risk of developing new-onset RA among WTC responders. Given the potential for respirators to reduce dust exposure and therefore RA risk, we investigated determinants of respirator use during the first week following 9/11 and compared respirator use to other surrogate measures of dust exposure such as site arrival time (i.e., morning of 9/11 vs. later), duration of work at the site, or location of work.

METHODS

Study Population

The study population consisted of 25,670 responders who participated in the WTC Health Program by enrolling in one of the five WTC clinical centers (NY/NJ WTC Consortium) at least once between July 16 2002 and December 31 2010. The WTC Health Program initially started as a medical screening program of workers and volunteers who worked at the WTC sites (lower Manhattan, the Staten Island landfill, barges and loading piers) for at least 4 hours from 9/11 to 9/14, at least 24 hours in the month of September, or at least 80 hours from 9/11 to the end of December 2001. Additional workers who were eligible included morgue workers and employees of the Office of the Chief Medical Examiner (OCME) and the Port Authority Trans-Hudson Corporation workers (Herbert 2006). Active firefighters and emergency medical services (EMS) workers of the Fire Department of the City of New York (FDNY) were served by a separate but similar health surveillance system, the FDNY WTC Health Program, and are not included in this analysis.

Study design

The NY/NJ WTC Consortium Health Program provided a longitudinal open enrollment cohort which began receiving baseline monitoring examinations on July 16, 2002 and allow enrolling the program anytime since then. Follow-up examinations were scheduled every 12 to 18 months. Active recruitment was performed by outreach activities to labor unions and by public advertisement. Program participation was voluntary and provided free medical screening and treatment for both physical and mental WTC-related conditions. Assessments included an interviewer-administered questionnaire and a standardized physical examination (Herbert 2006).

Arthritis information

General arthritis cases (all types of arthritis) were identified based on a positive response to the interviewer administered question: "Were you ever diagnosed with arthritis?" A following question asked the date of diagnosis. Incident cases were classified as having a diagnosis date from January 1 2002 through December 31 2010. This was the only arthritis question in the baseline examination; subsequent follow-up examinations included a question about the type of arthritis, with pre-selected types (i.e., rheumatoid, osteo-, psoriatic, post-traumatic, etc). An additional open-ended question recorded any other types of arthritis. Because of the absence of arthritis type at the baseline visit, we were not able to identify self-reported RA for those participants who were present only at the baseline examination. To address incomplete information on arthritis type, we created three case definitions with increasingly stringent criteria: Case I- all self-reported arthritis, which includes osteoarthritis (OA), RA, and any non-specific arthritis (NSA); Case II- all self-reported arthritis excluding OA reported at one or more follow up visits, which includes RA and NSA; and Case III- self-reported arthritis excluding both OA and NSA cases, i.e. those for which no specific information on the type was available, which leaves only RA. All three case definitions were fitted with the same regression model to facilitate comparison of their associations with WTC exposures.

Information on WTC dust exposures

WTC exposures were also assessed using an interviewer-administered questionnaire. Among the various exposure variables collected, we selected four major WTC exposures that potentially indicate the level of WTC dust/fumes inhaled or absorbed. First, arrival time to WTC site, categorized as: (1) arrived on 9/11 in the dust cloud, (2) arrived on 9/11 not in the dust cloud, and (3) arrived on 9/12 or later. Second, number of hours worked at WTC site in September, as a continuous variable. Third, location of work performed in September categorized as: (1) on the pile or in the pit, (2) adjacent to the pile or the pit, (3) landfill, (4) barges or loading piers, and (5) elsewhere, south of Canal St or the Office of the Chief Medical Examiner at 520 First Ave in Manhattan. These three WTC exposures have previously been described in detail (Woskie 2011). Lastly, we included the type of respiratory protection equipment used in 9/11-9/18 as three categories: (1) did not wear one, (2) nuisance dust/surgical/disposal masks, with a N95 to P100 rating at most, and (3) half-face or full-face respirator with replaceable filters/chemical cartridges/clean air supply (SCBA)/powered air purification (PAPR) (Antao 2011).

Demographics:

Pre-9/11 occupations were identified by asking "what was your trade/profession on 9/10/01?" Narrative text of these occupations have been cleaned and re-categorized using the Standard Occupational Classification (SOC) 2000 developed by the Bureau of Labor Statistics (BLS, 2015). Five major categories were used: (1) construction workers (SOC code: 47-000), (2) protective service workers (33-000), (3) electrical, telecommunications, & other installation & repair workers (49-000, abbreviated to "utility" from here), (4) Transportation and material movers (53-000, abbreviated to "transportation" from here"), and (5) business, engineering & administration (11-000, 13-000, 17-000, abbreviated to "business" from here). Details of pre-9/11 occupation have been previously reported (Woskie 2011). Other potential confounders included in the analysis were age at the baseline visit, sex, race, ethnicity, education, income, marital status, and cigarette smoking.

Statistical analysis:

Annual incidence rates of arthritis were estimated and presented by case definition and year of diagnosis. The risk of new-onset of arthritis was longitudinally compared using incidence rate ratios (IRRs) estimated by generalized estimating equations (GEEs) with the Poisson distribution and a log link (Barros 2003). To handle mild violations of the equidisperson assumption (underdispersion) of the Poisson distribution when the outcome variable is a binary or count response, the robust variance option in Stata was used (Cameron 2009). Crude and adjusted IRRs were compared and an exploratory analysis to identify factors associated with respirator use was performed. Crude and adjusted prevalence ratios (PRs) were calculated to investigate demographic factors and WTC exposures as determinants of respiratory use by a cross-sectional robust Poisson regression model with respirator use (yes/no) as the outcome.

All analyses were performed using Stata software version 11.2 (StataCorp LP). The study was approved by the Institutional Review Board of the Feinstein Institute for Medical Research at the North Shore-LIJ Health System. All study participants provided signed consent.

RESULTS

Descriptive characteristics:
Among the 25,670 total responders initially included in the analysis, a total of 5,648 prevalent arthritis cases were identified; 2,081 cases were pre-existing on 9/11/2001 and were excluded in the analysis.

The overall incidence rate for the period 2002 – 2010 19.0/1,000 person-years (Case I), 15.6/1,000 py (Case II), and 9.4/1,000 py (Case III) based on 3,542, 2,898 and 1,755 new cases of arthritis using definitions I, II and III respectively (Table 1).

Trends in annual incidence rates of arthritis varied depending on the case definition used. The incidence using Case I and II was highest in 2002, declined initially, rose around 2006, and fell thereafter. Using the Case III definition, incidence steadily decreased each year (Figure 1). The incidence rate for each case definition was 19.0 (Case I), 15.6 (Case II), and 9.4 (Case III) per 1000 person-years with incidence of 3,542 (case I), 2,898 (case II), and 1,755 (case III) per 186,111 total person-years. The majority of cases were male, white, non-Hispanic, with a median age of 47 years at the baseline visit, married or partnered, and reported never having smoked cigarettes (Table 1). With the exception of income, all demographic characteristics were differently distributed between cases (using any case definition) and the rest of the population ($p < 0.01$). Forty percent of responders were protective service workers and the other most common occupation was construction workers (19%). More than half of responders first worked after 9/11 and 95% began work in September. The median total working hours in September was 136 hours. Most cases reported that they worked on the pile/ pit (33%) and adjacent to the pile/pit (45%) in the month of September. A dust/surgical/disposal mask was used by 46% of cases, half/full-face respirator by 14%, and 19% of cases reported no respiratory protection.

Multivariate models of arthritis incidence
All demographic factors were strongly associated with the incidence of arthritis in either the crude or adjusted models, or both, using all case definitions ($p < 0.05$) (Table 2). The four WTC exposures included in the analysis, only half/full-face respirator use showed a statistically significant protective effect with all three case definitions of arthritis. Increased work hours in September at the WTC site had a marginal statistically significant association in Case I and II, but not with Case III. Missing category in the four WTC exposures also showed a significant association with arthritis, but further investigation of potential data error or unobserved bias is required.

Effect of alternative case definitions
We hypothesized that the protective effect of respirator usage would be stronger using a case definition that more closely captured rheumatoid arthritis and excluded other types. Thus the Case definition III which excluded OA and NSA would be expected to show a stronger association with respirator use (Figure 2). “Mask use” did not show differential strength of associations by case definitions and did not have a statistically significant association with any of three arthritis case definitions. This was different from “respirator use”, which did indeed have a protective effect. The types of masks and respirators are described previously.

Factors associated with respirator use
Because of this finding of evidence for a protective effect of respirator use, we explored potential determinants of respirator use in the first week of 9/11 (9/11-9/18) (Table 3). Reported respirator use did not vary importantly by race, ethnicity, or education once other variables were included in the model. Respirator use is reduced by age, among females, increased income, among singles, among current smokers, pre-9/11 occupations other than construction, among those who arrived to WTC site on 9/11, those who worked at the site less, and those who worked in September 2001 on the barges/loading piers/elsewhere. WTC responders who worked longer at the WTC site showed a tendency of more respirator use in both the crude and the adjusted models. Compared to construction occupation workers, all other occupations were significantly less likely to wear respirators. In particular, protective service workers were 65% less likely to wear respirators (PR=0.35 (0.33-0.38)), a surprising finding given the fact that protective service workers are among the traditional first-responder group together with firefighters.

DISCUSSION

Summary of main finding
While other auto-immune diseases have been reported among WTC responders, to our knowledge, this is the first study to assess increased incidence of potential rheumatoid arthritis among WTC responders (Moline 2009, Crowley 2011).

Although we were not able to select only rheumatoid arthritis from all arthritis cases reported due to the absence of arthritis type information at the baseline examination, we found a significant association between WTC exposure and potential rheumatoid arthritis when we used an arthritis definition which excluded osteoarthritis and non-specific arthritis. Among the four WTC exposures, wearing a half/full-face respirators in the first week of 9/11 (9/11-9/18) during their work at the WTC site showed a strong protective effect on the risk of developing potential rheumatoid arthritis (Case III) (IRR=0.66 (0.56-0.79)). This finding provides strong evidence in support of our study hypothesis that WTC dust, mainly silica and asbestos, can cause rheumatoid arthritis among WTC responders, and that respirator use may help mitigate this risk by effectively reducing dust inhalation.

Among WTC responders, only a few studies have reported of the association between respirator and mask use, and respiratory symptoms and diseases among WTC responders (Skloot 2004, Leinman 2011, Antao 2011). NYC WTC health registry researchers reported that half of the responders did not wear any respiratory protection and only one third wore unrated disposable masks; use of respirator masks increased to 50% after 1/1/2002 (Antao 2011). An early study (Skloot 2004) identified that 40% of ironworkers at the ground zero site wore no respiratory protection while 17% wore respirators; significantly fewer respiratory symptoms were reported among the respirator use group (OR=0.3).

We found that mask usage is negatively correlated with age, which receives mixed support from the literature (Fukakusa 2011), (White 1988), (Li 2002), (Schenker 2002). For gender, we found that males use respirators more than females (Reed 2006) and find them more comfortable (Baig 2010). Respirator use decreases with tobacco usage (Li 2002) which we also saw. We did not find supporting literature for the trend of respirator use being lower for higher income groups or for married or partnered workers.

To our knowledge, our study is the first to document an association between respirator use and potential rheumatoid arthritis. There is evidence to support our finding, as increased risk of rheumatoid arthritis in the presence of crystalline silica and asbestos exposure has been reported (Jones 2012, Hoovestol 2011, Stolt 2010, Stolt 2005, Khuder 2002, Parks 1999). Several government agencies and local public health groups conducted analyses of WTC dust shortly after 9/11 and found crystalline silica and asbestos in dust samples. Furthermore, the Ground Zero Task Force found significantly elevated levels of asbestos in dust and in the air from indoor samples immediately after 9/11 (Chatfield, 2001). New York City Department of Health and Mental Hygiene (NYCDOHMH) and Agency for Toxic Substances and Disease Registry (ASTDR) reported high levels of asbestos, fiberglass, crystalline silica from settled space dust in lower Manhattan (NYCDOHMH/ATSDR, 2002). The Environmental Protection Agency (EPA) also reported elevated level of asbestos in the ambient air samples in a few days after 9/11 (U.S. EPA 2004). Occupational Safety and Health Administration (OSHA) reported that 12 of 21 personal air samples from workers at Staten Island landfill exceeded OSHA permissible exposure limits (PEL). Landrigan (2004) also reported high levels asbestos, coarse cement particles, and glass fibers exposures in the first few hours after the disaster which remained at high levels for the next 2 days. This study also reported the large fraction of outdoor dust cleaning performed by 9/14 found still high levels of dust in the air over the next several weeks. This is an important indication as several studies have confirmed that while dust exposure was heaviest on the first day, exposure to crystalline silica and asbestos may have continued over several weeks. Webber (2015) also reported that prolonged exposure to dust, independent of acute exposure, was associated with post 9/11 systemic auto-immune diseases among a cohort of FDNY and EMS WTC first responders. Therefore, using proper respiratory protection in this early period might have significantly protected against rheumatoid arthritis onset among responders in spite of the high and prolonged levels of exposure.

Limitations and potential biases

Our findings should be interpreted in the context of several limitations. The main limitation of this study is the self-reported case definition and the absence of information on the type of arthritis at the baseline examination. Nearly half of the responders in this analysis completed only the baseline visit and as such we were not able to identify the type of arthritis among baseline only responders. To address this limitation, we developed two additional case definitions that excluded OA and both OA/NSA based on data collected from follow-up exams. This comparison shows clear pattern of stronger protective effect of respirator use after excluding potential non-rheumatoid arthritis.

Rheumatoid arthritis has a strong genetic component (Nepom 1989, Wordsworth 1989, Ronningen 1990, Fries 2002) which we were not able to evaluate or control. We did investigate other known risk factors including age, gender, smoking, and socioeconomic status. All of these risk factors showed the expected associations with the restricted definition of arthritis. These factors did not, however, explain the observed association between respirator use and rheumatoid arthritis.

Among WTC exposures, we were particularly interested in reported arrival time to the WTC site because this variable has been the only predictor of most WTC related health problems reported and has been used by other investigators as a surrogate for the amount of dust exposure [ref]. Initially, we hypothesized that arriving on that day in the dust cloud would increase arthritis incidence due to a greater amount of WTC dust exposure, but we found no clear evidence for this. The association between rheumatoid arthritis and the missing category for information on respirator use requires further investigation; there may be an underlying systematic clustering of a unique group of people who did not provide this information and for other reasons have a lower risk of arthritis. Investigating this further may require substantial effort including verification of the paper questionnaires of historical data over 10 years.

Other potential biases discussed in the context of WTC cohorts include self-selection and recall biases. It is possible that sicker responders may have been more likely to enroll in the WTC Health Program in the early period and also attend follow-up exams more frequently. We found that arthritis incidence was highest in 2002 then declined drastically in 2010 (Figure 1). This may be partial evidence that, at least with arthritis, less health responders participated in the WTC program earlier and less sick or healthy responders may have enrolled later (or not even enrolled) in the program. The self-selection bias can be minimized if the cohort recruited close to all of the exposed population. Savitz predicted that approximately 40,000 people responded or volunteered to 9/11. If the prediction is true, 36% of eligible responders may not have enrolled which may have an effect on the associations in our analysis. If those not included have an inverse association from what we observed (i.e., respirator use increased arthritis risk), our findings may be severely biased. However we believe that the likelihood of observing an inverse association would be very low, as the association we observed is well supported from previous literature.

Recall bias can be critical in this analysis because the WTC program is an open cohort and responders can enroll in the program at any time, which requires remembering events from 10 years ago or more. Remembering the type of respiratory protection used within a specific period (9/11-9/18) can be a great challenge among those enrolled in later years. In general, less sick or healthy people are less likely to remember their exposure (unintentional recall bias). Also people may be less likely to report respirator use if there is any disadvantage associated with use of respiratory protection (intentional recall bias). We found that arthritis cases in our study less likely reported respirator use which may indicate some “intentional recall bias”. However the association between arthritis and respirator is not widely known; thus, we believe the chance of this intentional recall bias of arthritis cases reporting more/less use of respirator masks would be less likely.

In conclusion, we found a strong protective effect of potential rheumatoid arthritis incidence when respirator masks were used among WTC responders. Our finding strongly supports the use of respirators in reducing the risk of developing rheumatoid arthritis among first responders and general construction workers who may work in similar situations. In addition to rheumatoid arthritis, other autoimmune diseases among the responders such as sarcoidosis and multiple myeloma as well as un-reported autoimmune diseases should be explored to confirm the protective effects of respirator use among responders in the WTC disaster. Programmatic efforts focused on the use of respirator masks and its benefits may help mitigate the health consequences of exposure to toxic substances among first responders during disasters.

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Table 1. Characteristics of responders with self-reported physician diagnosed arthritis by three case definitions

Variable	Case I (n=3,542)		Case II (n=2,898)		Case III (n=1,755)		Total (n=27,261)	
Age at the baseline visit								
20-29	53	(1.5)	46	(1.6)	13	(0.7)	1,301	(4.8)
30-39	674	(19.0)	553	(19.1)	305	(17.4)	8,743	(32.1)
40-49	1,492	(42.1)	1,205	(41.6)	702	(40.0)	11,127	(40.8)
50-59	1,011	(28.5)	824	(28.4)	548	(31.2)	4,843	(17.8)
60+	312	(8.8)	270	(9.3)	187	(10.7)	1,247	(4.6)
Sex								
Male	2,852	(80.5)	2,340	(80.8)	1,408	(80.2)	23,292	(85.4)
Female	690	(19.5)	558	(19.3)	347	(19.8)	3,969	(14.6)
Race								
White	2,185	(61.7)	1,787	(61.7)	1,107	(63.1)	16,056	(58.9)
Black	414	(11.7)	331	(11.4)	178	(10.1)	3,001	(11.0)
Asian	37	(1.0)	30	(1.0)	19	(1.1)	380	(1.4)
Other	93	(2.6)	67	(2.3)	42	(2.4)	780	(2.9)
Unknown	813	(23.0)	683	(23.6)	409	(23.3)	7,044	(25.8)
Ethnicity								
Hispanic	777	(21.9)	648	(22.4)	369	(21.0)	6,449	(23.7)
Non-Hispanic	2,091	(59.0)	1,696	(58.5)	993	(56.6)	15,126	(55.5)
Unknown	674	(19.0)	554	(19.1)	393	(22.4)	5,686	(20.9)
Education								
Some or graduated from high school	1,172	(33.1)	970	(33.5)	586	(33.4)	8,327	(30.6)
Two year college	1,290	(36.4)	1,056	(36.4)	622	(35.4)	10,528	(38.6)
Graduated from college or graduate school	1,080	(30.5)	872	(30.1)	547	(31.2)	8,406	(30.8)
Income*								

<$30,000	298	(8.4)	242	(8.4)	139	(7.9)	2,419	(8.9)
$30-60,000	801	(22.6)	650	(22.4)	393	(22.4)	6,222	(22.8)
$60-80,000	811	(22.9)	649	(22.4)	413	(23.5)	6,155	(22.6)
>$80,000	885	(25.0)	737	(25.4)	448	(25.5)	6,859	(25.2)
Missing	747	(21.1)	620	(21.4)	362	(20.6)	5,606	(20.6)
Marital status								
Single	462	(13.0)	378	(13.0)	218	(12.4)	4,147	(15.2)
Married or partnered	2,423	(68.4)	1,962	(67.7)	1,199	(68.3)	18,429	(67.6)
Separated or divorced	608	(17.2)	512	(17.7)	299	(17.0)	4,086	(15.0)
Widowed	49	(1.4)	46	(1.6)	39	(2.2)	599	(2.2)
Cigarette smoking								
Never	1,865	(52.7)	1,550	(53.5)	951	(54.2)	15,586	(57.2)
Current smoker	471	(13.3)	386	(13.3)	241	(13.7)	3,963	(14.5)
Former smoke	948	(26.8)	770	(26.6)	477	(27.2)	6,181	(22.7)
Missing	258	(7.3)	192	(6.6)	86	(4.9)	1,531	(5.6)
Pre-9/11 occupation								
Construction	675	(19.1)	552	(19.1)	331	(18.9)	5,347	(19.6)
Protective service	1,335	(37.7)	1,104	(38.1)	702	(40.0)	11,979	(43.9)
Utility	240	(6.8)	192	(6.6)	128	(7.3)	1,627	(6.0)
Transportation	160	(4.5)	132	(4.6)	77	(4.4)	999	(3.7)
Business	460	(13.0)	380	(13.1)	228	(13.0)	3,319	(12.2)
Other	672	(19.0)	538	(18.6)	289	(16.5)	3,990	(14.6)
Arrival to WTC site								
After 9/11	1,845	(52.1)	1,522	(52.5)	922	(52.5)	14,793	(54.3)
On 9/11 not in the dust cloud	738	(20.8)	605	(20.9)	385	(21.9)	6,030	(22.1)

On 9/11 in the dust cloud	667	(18.8)	551	(19.0)	332	(18.9)	5,076	(18.6)
Missing	292	(8.2)	220	(7.6)	116	(6.6)	1,362	(5.0)
Hours of work in Sept								
Median (Interquatile range)	120	(36-216)	120	(36-216)	119	(40-216)	136	(48-227)
Type of respiratory protection used in 9/11-9/18								
Didn't wear one	623	(17.6)	518	(17.9)	341	(19.4)	4,491	(16.5)
Dust/ surgical/ disposable mask	1,557	(44.0)	1,288	(44.4)	801	(45.6)	12,092	(44.4)
Half/full-face respirator	558	(15.8)	461	(15.9)	244	(13.9)	4,738	(17.4)
Other/don't know/missing	403	(11.4)	315	(10.9)	187	(10.7)	2,943	(10.8)
Not in the period (9/11-9/18)	401	(11.3)	316	(10.9)	182	(10.4)	2,997	(11.0)
Location of work in September 2001								
On the pile/in the pit	1,174	(33.2)	967	(33.4)	584	(33.3)	9,148	(33.6)
Adjacent to pile/pit	1,587	(44.8)	1,304	(45.0)	782	(44.6)	12,312	(45.2)
Landfill	75	(2.1)	67	(2.3)	46	(2.6)	705	(2.6)
Barges/Loading piers	40	(1.1)	28	(1.0)	17	(1.0)	264	(1.0)
Elsewhere	271	(7.7)	222	(7.7)	145	(8.3)	1,902	(7.0)
Don't know/missing	395	(11.2)	310	(10.7)	181	(10.3)	2,930	(10.8)

Note: Case I=all arthritis types; Case II=excluding osteoarthritis; Case III=excluding osteoarthritis and non-specific arthritis type reported

*not statistically significant between cases and non-cases at the level alpha=0.05.

Table 2. Crude and adjusted arthritis incidence rate ratios (IRRs) and comparison of models by the three case definitions

Variable	Crude			Adjusted								
	Case III (n=3,542)			Case I (n=3,542)			Case II (n=2,898)			Case III (n=1,755)		
	IRR	95% CI		IRR	95% CI		IRR	95% CI		IRR	95% CI	
Age at the baseline visit												
20-29	1			1			1			1		
30-39	3.60	2.07	6.28	1.91	1.44	2.54	1.79	1.32	2.44	3.36	1.93	5.88
40-49	6.73	3.88	11.66	3.39	2.56	4.49	3.12	2.31	4.22	6.20	3.56	10.77
50-59	12.73	7.34	22.08	5.61	4.23	7.44	5.21	3.85	7.07	12.31	7.07	21.44
60+	17.90	10.19	31.45	7.34	5.44	9.90	7.14	5.17	9.85	17.62	9.98	31.11
Sex												
Male	1			1								
Female	1.57	1.39	1.76	1.67	1.52	1.83	1.61	1.45	1.79	1.76	1.54	2.01
Race												
White	1			1			1			1		
Black	0.90	0.77	1.05	0.95	0.85	1.05	0.92	0.82	1.04	0.78	0.66	0.92
Asian	0.70	0.45	1.11	0.77	0.56	1.07	0.78	0.54	1.12	0.81	0.51	1.28
Other	0.76	0.55	1.03	0.90	0.72	1.13	0.80	0.61	1.04	0.86	0.61	1.21
Unknown	0.94	0.84	1.05	0.97	0.85	1.11	1.00	0.86	1.16	1.05	0.87	1.26
Ethnicity												
Hispanic	1			1			1			1		
Non-Hispanic	1.09	0.96	1.23	0.99	0.86	1.14	0.97	0.82	1.13	1.03	0.84	1.26
Unknown	1.41	1.23	1.63	0.97	0.85	1.11	0.97	0.83	1.12	1.24	1.02	1.50
Education												
Some or graduated from high school	1			1								
Two year college	0.85	0.76	0.95	0.93	0.85	1.01	0.92	0.83	1.01	0.88	0.78	1.00
College or graduate school	0.95	0.84	1.07	0.92	0.84	1.00	0.89	0.80	0.98	0.90	0.79	1.02
Income												
<$30,000	1			1			1.00			1.00		
$30-60,000	1.12	0.92	1.36	1.13	0.98	1.30	1.14	0.98	1.34	1.15	0.93	1.41
$60-80,000	1.19	0.98	1.44	1.18	1.02	1.36	1.18	1.00	1.39	1.21	0.98	1.50
>$80,000	1.15	0.95	1.39	1.14	0.98	1.32	1.19	1.01	1.41	1.15	0.92	1.44
Missing	1.17	0.96	1.42	1.12	0.97	1.29	1.17	0.99	1.37	1.11	0.90	1.37
Marital status												
Single	1			1			1.00			1.00		
Married or partnered	1.22	1.06	1.41	1.02	0.92	1.14	1.00	0.89	1.12	1.01	0.86	1.17
Separated or divorced	1.40	1.17	1.66	0.99	0.88	1.12	1.01	0.88	1.16	0.96	0.80	1.15
Widowed	1.66	1.18	2.34	0.76	0.57	1.02	0.89	0.65	1.21	1.29	0.91	1.83
Cigarette smoking												
Never	1			1			1.00			1.00		

Current smoker	1.02	0.88	1.17	1.00	0.90	1.12	0.99	0.88	1.11	1.02	0.88	1.18
Former smoke	1.27	1.13	1.41	1.06	0.97	1.15	1.02	0.94	1.12	0.98	0.87	1.10
Missing	0.94	0.76	1.17	1.00	0.85	1.17	0.92	0.76	1.11	0.65	0.49	0.86
Pre-9/11 occupation												
Construction	1			1								
Protective service	1.04	0.92	1.19	1.00	0.89	1.12	1.02	0.90	1.16	1.06	0.91	1.25
Utility	1.31	1.06	1.61	1.13	0.97	1.32	1.11	0.94	1.31	1.17	0.95	1.44
Transportation	1.36	1.06	1.74	1.19	1.00	1.42	1.20	0.99	1.46	1.09	0.84	1.41
Business	1.19	1.00	1.41	0.97	0.85	1.10	0.98	0.85	1.13	0.90	0.75	1.08
Other	1.16	0.99	1.36	1.05	0.93	1.18	1.05	0.92	1.20	0.93	0.78	1.11
Arrival to WTC site												
After 9/11	1			1			1.00			1.00		
On 9/11 not in the dust cloud	1.02	0.91	1.15	1.04	0.94	1.14	1.02	0.92	1.13	1.04	0.91	1.18
On 9/11 in the dust cloud	1.02	0.90	1.16	1.08	0.98	1.19	1.07	0.96	1.19	1.03	0.90	1.18
Missing	1.31	1.08	1.59	1.61	1.37	1.89	1.51	1.26	1.81	1.47	1.15	1.87
Hours of work in Sept (per 100 hours)	0.91	0.86	0.96	0.96	0.92	1.00	0.94	0.90	0.99	0.96	0.90	1.01
Type of mask used in 9/11-9/18												
Didn't wear one	1			1								
Dust/ surgical/ disposable mask	0.84	0.74	0.95	0.95	0.87	1.05	0.94	0.85	1.05	0.91	0.80	1.03
Half/full-face respirator	0.58	0.49	0.68	0.82	0.73	0.92	0.81	0.71	0.92	0.66	0.56	0.79
Other/don't know/missing	0.79	0.66	0.94	0.88	0.76	1.01	0.84	0.72	0.98	0.81	0.67	0.99
Not in the period (9/11-9/18)	0.74	0.62	0.89	0.95	0.82	1.11	0.87	0.73	1.03	0.75	0.60	0.94
Location of work in September 2001												
On the pile/ in the pit	1			1								
Adjacent to pile/ pit	1.00	0.90	1.12	0.93	0.86	1.01	0.93	0.86	1.02	0.94	0.84	1.05
Landfill	1.05	0.77	1.42	0.73	0.58	0.93	0.80	0.62	1.03	0.89	0.65	1.20
Barges/ Loading piers	1.00	0.62	1.63	0.92	0.67	1.27	0.78	0.54	1.14	0.75	0.46	1.22
Elsewhere	1.26	1.05	1.51	0.94	0.82	1.08	0.94	0.81	1.10	0.95	0.79	1.15
Don't know/missing	0.99	0.83	1.17	0.80	0.69	0.93	0.81	0.68	0.96	0.87	0.71	1.08

Note: Case I=all arthritis types; Case II=excluding osteoarthritis; Case III=excluding osteoarthritis and non-specific arthritis type reported; Person-time defined from enrollment to diagnosis date or last follow-up.

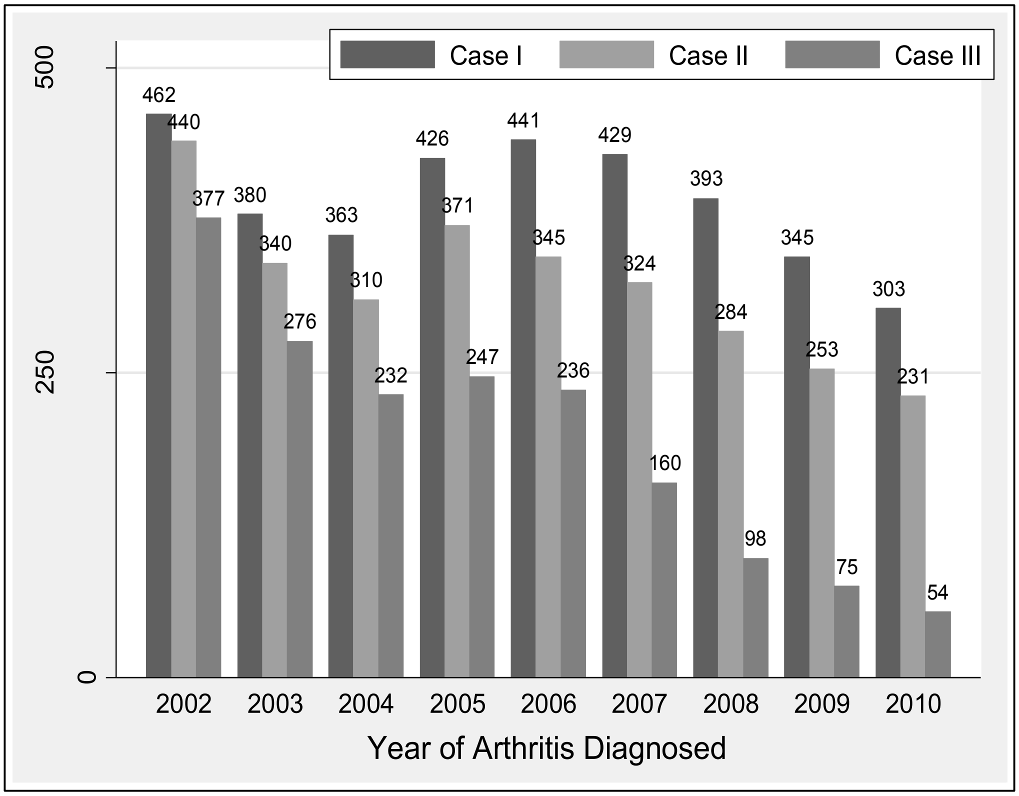

Figure 1. Annual arthritis incidence by three case definitions

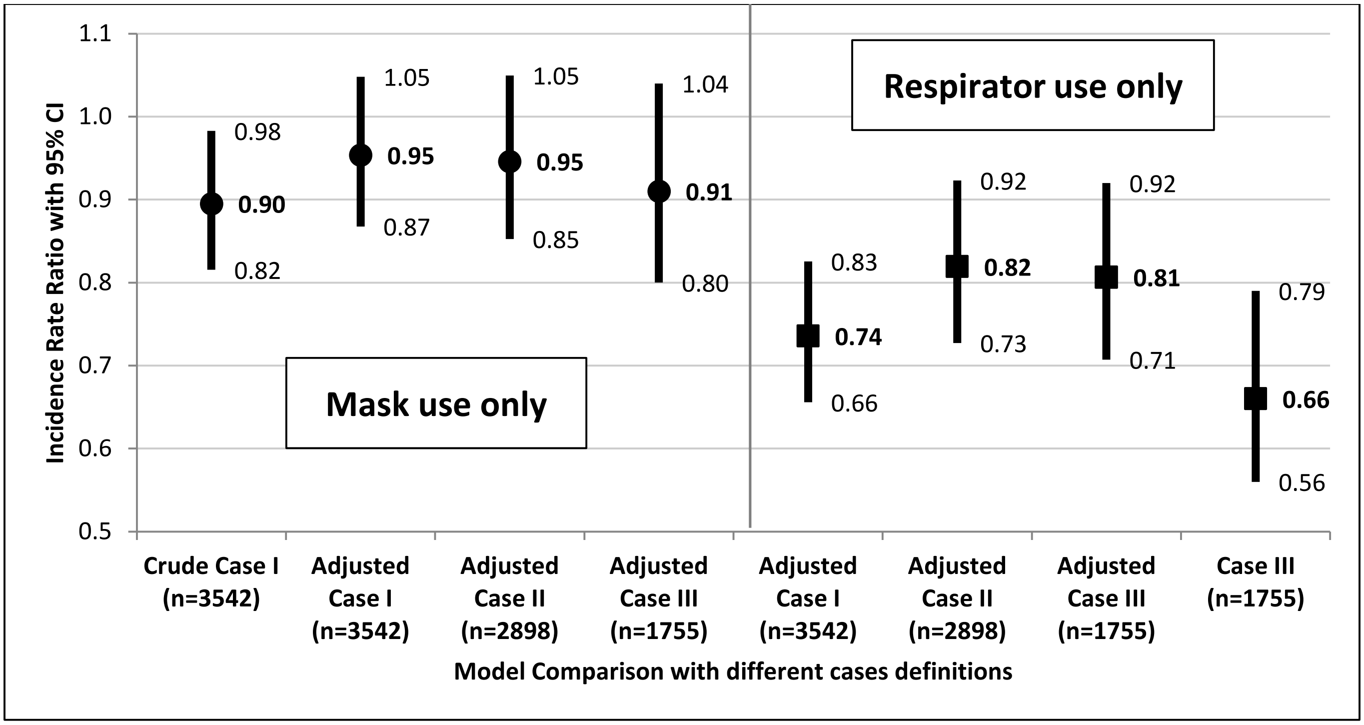

Figure 2. Crude and adjusted arthritis incidence rate ratio by three case definitions and by mask and respirator use.

Table 3. Respirator use in 9/11-9/18 and corresponding prevalence ratios (PRs) (N=4,738).

Demographic characteristics and WTC exposures	Respirator used n (%)*	Crude PR			Adjusted PR		
		PR	95% CI		PR	95% CI	
Age at the baseline visit							
20-29	295 (28.2)	1			1		
30-39	1577 (19.9)	0.70	0.63	0.78	0.95	0.86	1.05
40-49	1803 (18.0)	0.64	0.57	0.71	0.88	0.79	0.97
50-59	859 (20.5)	0.73	0.65	0.81	0.89	0.80	0.99
60+	204 (19.7)	0.70	0.60	0.82	0.81	0.70	0.94
Sex							
Male	4258 (20.3)	1			1		
Female	480 (14.6)	0.72	0.66	0.79	0.76	0.70	0.83
Race							
White	2747 (18.7)	1			1		
Black	445 (16.6)	0.89	0.81	0.98	0.93	0.85	1.02
Asian	54 (15.8)	0.85	0.66	1.09	0.95	0.75	1.22
Other	154 (22.7)	1.21	1.05	1.40	1.10	0.95	1.27
Unknown	1338 (22.8)	1.22	1.15	1.29	1.07	0.96	1.18
Ethnicity							
Hispanic	1320 (24.9)	1			1		
Non-Hispanic	2714 (19.8)	0.79	0.75	0.84	0.99	0.89	1.10
Unknown	704 (13.5)	0.54	0.50	0.59	0.78	0.71	0.87
Education							
Some or graduated from high school	1732 (24.7)	1			1		
Two year college	1689 (17.5)	0.71	0.67	0.75	0.98	0.93	1.04
College or graduate school	1317 (17.3)	0.70	0.66	0.75	1.04	0.98	1.11
Income							
<$30,000	630 (37.0)	1			1		
$30-60,000	1092 (19.6)	0.53	0.49	0.58	0.74	0.69	0.80
$60-80,000	900 (15.7)	0.43	0.39	0.46	0.69	0.63	0.75
>$80,000	1120 (17.3)	0.47	0.43	0.51	0.74	0.68	0.80
Missing	996 (20.8)	0.56	0.52	0.61	0.79	0.73	0.85
Marital status							
Single	669 (18.6)	1			1		
Married or partnered	3275 (19.7)	1.06	0.99	1.15	1.08	1.01	1.17
Separated or divorced	712 (20.2)	1.09	0.99	1.20	1.05	0.96	1.15
Widowed	82 (15.6)	0.84	0.68	1.03	0.86	0.71	1.04
Cigaret smoking							
Never	2689 (19.2)	1			1		
Current smoker	771 (22.5)	1.17	1.09	1.26	0.90	0.84	0.97

Former smoke	1124 (20.8)	1.08	1.02	1.15	0.98	0.92	1.04
Missing	154 (10.7)	0.55	0.48	0.65	0.86	0.74	1.00
Pre-9/11 occupation							
Construction	1716 (40.6)	1			1		
Protective service	1396 (12.1)	0.30	0.28	0.32	0.35	0.33	0.38
Utility	358 (25.0)	0.62	0.56	0.68	0.68	0.62	0.75
Transportation	114 (12.9)	0.32	0.27	0.38	0.36	0.30	0.43
Bussiness	522 (19.2)	0.47	0.43	0.51	0.56	0.51	0.61
Other	632 (18.1)	0.45	0.41	0.48	0.58	0.54	0.63
Arrival to WTC site							
After 9/11	2991 (25.3)	1			1		
On 9/11 not in the dust cloud	893 (14.8)	0.58	0.55	0.63	0.73	0.68	0.78
On 9/11 in the dust cloud	770 (15.2)	0.60	0.56	0.64	0.75	0.69	0.80
Missing	84 (6.2)	0.25	0.20	0.30	0.44	0.35	0.56
Hours of work in Sept (in 100 hours)	**171 (152)****	1.13	1.11	1.15	1.16	1.14	1.19
Location of work in September 2001							
On the pile/ in the pit	1680 (18.8)	1			1		
Adjacent to pile/ pit	2665 (23.6)	1.25	1.19	1.32	1.06	1.00	1.12
Landfill	120 (18.4)	0.98	0.83	1.15	1.31	1.11	1.55
Barges/ Loading piers	20 (8.0)	0.42	0.28	0.65	0.46	0.30	0.70
Elsewhere	170 (9.4)	0.50	0.43	0.58	0.59	0.50	0.68
Don't know/missing	83 (6.3)	0.33	0.27	0.41	0.52	0.41	0.66

*n (%)=number of WTC responders who used respirator (percent of respirator used among total N in each category)

**n(n)=Median hours among respirator used (median hours among not respirator used)

Appendix 8
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SOCIOECONOMIC STATUS AND ASTHMA AMONG WTC RESPONDERS.

Hyun Kim, Marlene Camacho, Francine Smith, Sherry Baron, David Kriebel, Jacqueline Moline

Although studies have reported health problems among WTC responders, the consequent socioeconomic impact has not been studied. We investigated whether WTC responders diagnosed with Asthma were more likely to experience a change in their full-time job status. Job status change from full-time to lower status (part-time, disabled, laid off, or retired) was used as a surrogate of lowered socioeconomic status (SES). Only responders who had at least 2 visits and held full-time status at visit 1 were included. Association with asthma was assessed after adjusting for known risk factors of socioeconomic status. Stratified modeling by asthma status was performed with robust Poisson regression. Among total 26,768 responders who participated the WTC Health Program by 2010, 8,132 responders met the inclusion criteria and included in the analysis. Asthma incidence was 5 per 100 responders. 41% with asthma and 33% without asthma lost their full-time status since the first visit. 8% changed to disabled, 15% were laid off/unemployed, 36% retired/became students and 41% changed to part-time. Asthma was strongly associated with status changed to disabled (Incidence rate ratio (IRR)=1.86(1.13-3.06)) followed by changed to retired (IRR=1.40(1.12- 1.75)) and changed to any lower status (IRR=1.24(1.09-1.42)). Stratified analysis by asthma showed significant associations with only WTC exposures when responders developed asthma since 9/11 while only demographic factors were associated with job status changes among non-asthmatics. Our study found that asthma was an independent determinant of job status changes among WTC responders and no demographic characteristic affected job status changes if responders developed asthma. It is possible that asthma plays a role of mediator between WTC exposures and job status changes if asthma was a consequence of WTC exposure. Lowered SES should be considered as an important adverse effect of WTC exposure, especially when lowering SES impacts developing health problems.

Appendix 9

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Health effect of the WTC disaster among responders: 10 years assessment

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Keywords: 9/11 disaster, first responders, asthma

Introduction

Overall health status of WTC responders after 10 years from the 9/11 disaster was evaluated by comparing prevalence of five major health outcomes to the general population surveyed by the National Health Interview Survey (NHIS). Potential associations between new onset of asthma and WTC exposures were investigated, especially the protective effect of respirator use during rescue and recovery activities.

Methods

A total of 26,796 responders who participated in the WTC Health Program (WTCHP) from 2002-2010 were included in the analysis. Standardized Morbidity Ratios (SMR) for asthma, hypertension, diabetes, cancer, and stroke were calculated after adjusting for age and occupation, separately, and stratified by gender. Self-reported life-time prevalence of each outcome was used for SMR. Internal comparison was conducted for asthma incidence. Incidence Rate Ratios (IRR) were estimated using the generalized estimating equations with robust Poisson family and log link.

Results

Among the five health outcomes compared with NHIS, asthma was the only outcome showing an elevated rate. From the internal comparison, protective service (IRR=1.31 (1.12-1.54)) and utility workers (IRR=1.39 (1.11-1.73) had a higher risk of experiencing asthma compared to construction workers. Responders who arrived at the site on 9/11 not in the dust cloud (IRR=0.81 (0.71-0.93)) or later had a lower risk of getting asthma than those who arrived on 9/11 in the dust cloud. Notably, responders who used a full/half-face respirator on 9/11-9/18 had a significantly lower risk (IRR=0.70 (0.60-0.82) than when none was worn.

Discussion

We confirmed that asthma was the main health problem among WTC responders and we did not observe an increased risk of the other four health outcomes. We also found a clear protective effect of using a respirator on asthma incidence. This is an important finding not only for future disaster preparedness but also for protecting general workers from their daily occupational exposures.