A. OVERALL COVER PAGE

Project Title: Maintenance and Extension of a Cohort of Career Firefighters as a Non-WTC Exposed Comparison for the FDNY Firefighter Cohort	
Grant Number: 5U01OH011934-03	**Project/Grant Period:** 01/01/2019 - 08/31/2023
Reporting Period: 09/01/2020 - 08/31/2023	**Requested Budget Period:** 09/01/2020 - 08/31/2021
Report Term Frequency: Final	**Date Submitted:** 12/26/2023
Program Director/Principal Investigator Information: MAYRIS P WEBBER , DRPH MPH DRPH MPH **Phone Number:** 718 920-4151 **Email:** mwebber@montefiore.org	**Recipient Organization:** ALBERT EINSTEIN COLLEGE OF MEDICINE 1300 MORRIS PARK AVE BRONX, NY 104611900 **DUNS:** 081266487 **UEI:** H6N1ZF5HJ2G3 **EIN:** 1830621846A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: ROSE RAMUNNO 1300 Morris Park Avenue Bronx, NY 10461 **Phone number:** 718-430-8846 **Email:** rose.ramunno@einsteinmed.edu	**Signing Official:** ROSE RAMUNNO 1300 Morris Park Avenue Bronx, NY 10461 **Phone number:** 718-430-8846 **Email:** rose.ramunno@einsteinmed.edu
Human Subjects: NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goals of this 5-year proposal are as follows:
Aim 1: Determine whether firefighters in the FDNY FF Cohort have higher cancer incidence rates than firefighters in the FF Comparison Cohort. We will compare cancer incidence rates in the FDNY FF Cohort for all cancers and for common individual cancers, as obtained from linkages to all relevant State Cancer Registries (which will be performed as part of another cooperative agreement), to the incidence rates observed in the FF Comparison Cohort (linkages to this cohort performed under this cooperative agreement).
Aim 2: Establish a well-characterized cohort of firefighters from the FF Comparison Cohort for lifelong follow-up. This cohort will be selected by comparability to the FDNY FF Cohort in age on 9/11, years of firefighter service, and race/ethnicity for follow-up surveys
(web- based and telephone) every 2 years. This aim will be completed by RTI International.
Aim 3: Compare the post-9/11 prevalence and incidence of physical and mental health symptoms and diagnosed conditions in the FDNY FF Cohort and the FF Comparison Cohort. These survey data will be obtained from participants from the FF Comparison Cohort via completion of biannual surveys. FDNY firefighters currently complete similar surveys during their routine medical monitoring visits. We will start by ascertaining the baseline prevalence of common chronic conditions (e.g., asthma, GERD) in both cohorts and follow up by comparing the annual incidence of these conditions over time.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : Final CFHS closeout report.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We have provided study results to each of the fire departments included in the study.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

Title Page

Title: Maintenance and Extension of a Cohort of Career Firefighters as a Non-WTC Exposed Comparison for the FDNY Firefighter Cohort
Grant number: National Institute of Occupational Safety and Health grant U01 OH011309/U01 OH011934

Institution:
Albert Einstein College of Medicine, 1301 Morris Park Avenue, Bronx, NY 10461

Principal Investigator:
Mayris Webber, DrPH

Project Start Date: 9/1/2016
Project End Date: 8/31/2023 (2nd NCE)

Final Report Date: 11/29/2023

Table of Contents

List of Terms and Abbreviations

WTC = World Trade Center
FDNY=Fire Department of the City of New York
CFHS = Career Firefighter Health Study

Abstract

Title: Maintenance and Extension of a Cohort of Career Firefighters as a Non-WTC Exposed Comparison for the FDNY Firefighter Cohort

PI: Mayris Webber DrPH, MPH

Background

Studies of World Trade Center (WTC)-exposed rescue/recovery workers report the increased occurrence of health conditions after work at the WTC disaster site. However, the extent to which these associations are due to WTC exposure is unclear, in part due to the lack of suitable comparison groups. Accordingly, we identified a previously assembled National Institute for Occupational Safety and Health (NIOSH) cohort of career firefighters from Chicago, Philadelphia, and San Franscico (n=29,992). The cohort was renamed the Career Firefighter Health Study, and the Fire Department of the City of New York (FDNY) firefighters were added.

Methods

Follow-up process included institutional review board applications, data use agreements, 15 state cancer registry linkages and National Death Index linkage. After completion of these steps, we undertook outreach to the Chicago, Philadelphia, and San Franscico fire departments and union officials, prior to contact tracing and direct recruitment of 14,566 living firefighters to complete a confidential health survey. The health survey included both physical and mental health questions and was modeled off the FDNY health surveys. We staggered recruitment efforts by city, using letters, postcards, emails, videos and telephone outreach. Analyses compared FDNY WTC-exposed firefighters with non-exposed firefighters from the other three cities.

Results

We identified 915 cancer cases in 841 FDNY firefighters and 1,002 cases in 909 CFHS firefighters. FDNY had: higher rates for all-cancers (RR=1.13; 95%CI=1.02-1.25), prostate (RR=1.39; 95%CI=1.19-1.63), and thyroid cancer (RR=2.53; 95%CI=1.37-4.70); younger median ages at diagnosis (55.6 vs. 59.4; p<.001, all-cancers); and more cases with localized disease when compared with CFHS. WTC-exposed firefighters had lower rates of all-cause and cancer-, heart disease- and respiratory disease-specific mortality compared with non-WTC-exposed firefighters.

A total of 4,962 of 14,566 alive firefighters from Chicago, Philadelphia, and San Franscico responded to the baseline survey (34.1% response rate). Results from the survey found differences between FDNY WTC-exposed firefighters and non-WTC-exposed firefighters when assessing self-reported health outcomes. WTC-exposure was associated with fewer subjective cognitive concerns (β=-0.69±0.05, p<0.001) after controlling for covariates Odds of any self-reported obstructive airway disease and asthma specifically, were 4.5 and 6.3 times greater, respectively, in WTC-exposed vs. non-WTC-exposed. Greater WTC exposure was positively associated with combined self-reported coronary artery disease, myocardial infarction, and angina when comparing WTC-exposed to non-WTC-exposed firefighters.

Conclusions

By expanding maintaining and updating the Career Firefighter Health Study cohort, we have created a valuable comparison cohort for the WTC-exposed firefighters. With this comparison, we found WTC-exposed firefighters have a greater incidence of cancer compared with non-exposed firefighters, but their risk of mortality is lower. Further, we found WTC-exposed firefighters reported more physical health diagnoses than non-exposed firefighters. The Career Firefighter Health Study cohort and survey can beneficial for future WTC studies as well as firefighting studies.

Section 1 of the Final Progress Report

Significant or Key Findings

Hundreds of studies of World Trade Center (WTC)-exposed rescue/recovery workers and others have documented the incidence and prevalence of conditions that are thought to occur more commonly as a consequence of exposure to the WTC disaster site. Fire Department of the City of New York (FDNY) WTC-exposed firefighters had higher rates for all-cancers, prostate, and thyroid cancer compared with non-WTC-exposed firefighters from Chicago, Philadelphia and San Francisco. WTC-exposed firefighters had lower rates of all-cause and cancer-, heart disease- and respiratory disease-specific mortality compared with non-WTC-exposed firefighters. Results from the survey found differences between FDNY WTC-exposed firefighters and non-WTC-exposed firefighters when assessing self-reported health outcomes. WTC-exposure was associated with fewer subjective cognitive concerns after controlling for covariates. Odds of any self-reported obstructive airway disease was over four-fold greater in WTC-exposed compared with non-WTC-exposed. Greater WTC exposure was positively associated with self-reported cardiovascular disease when comparing WTC-exposed to non-WTC-exposed firefighters.

Translation of Findings

These findings support prior findings that that World Trade Center exposure is associated with diagnoses of physical health conditions including cancer, obstructive airway disease and cardiovascular disease, though now with the ability to control for the confounding due to healthy worker effect and firefighting exposures.

Research Outcomes/Impact

The findings from this study provides insight into the WTC related conditions while controlling for the health worker effect and other occupational exposures.

Section 2 of the Final Progress Report

Scientific Report

Aim 1

Determine whether firefighters in the FDNY Firefighter Cohort have higher cancer incidence rates than firefighters in the Firefighter Comparison Cohort.

Cancer Incidence in World Trade Center-Exposed and Non-Exposed Male Firefighters, as Compared with the US Adult Male Population: 2001 - 2016

Mayris P. Webber, DrPH, Ankura Singh, MPH, Rachel Zeig-Owens, DrPH, Joke Salako, MPH, Molly Skerker, MPH, Charles B. Hall, PhD, David G. Goldfarb, MPH, Nadia Jaber, RPA-C, David J. Prezant, MD

Introduction

Firefighters are repeatedly exposed to occupational hazards, including known carcinogens.[1, 2] There have been over 200 peer-reviewed studies of firefighting and cancer, shown in PubMed,[3-9] most published since 2000. Despite this proliferation of studies, the degree to which firefighting is associated with cancer incidence remains uncertain. A 2014 National Institute for Occupational Safety and Health (NIOSH) study found that a cohort of ~30,000 professional firefighters had a modest elevation in the rate of all-cancers combined (standardized incidence ratio [SIR]=1.09; 95% CI=1.06-1.12) compared with the general US population.[4] A recent meta-analysis of 25 cohort studies, including the aforementioned NIOSH cohort, however, reported that the all-cancer risk for firefighters was similar to that of the general population (meta-relative risk [mRR]=1.0; 95% CI=0.93-1.07).[10]

The World Trade Center (WTC) attacks on 11/9/2001 (9/11) exposed ~13,000 Fire Department of the City of New York (FDNY) firefighters and other rescue/recovery workers to carcinogenic substances[11-13] including PCBs, PAHs, asbestos, sulfuric acid, benzene and arsenic.[2, 13, 14] Studies of WTC-exposed rescue/recovery workers have generally shown modestly elevated cancer rates compared with general populations.[15-19]

The current study was undertaken to assess if work as an FDNY firefighter at the WTC site conferred a cancer risk above that attributed to firefighting under non-WTC conditions. Our 2016 study[20] compared post-9/11 cancer incidence in the FDNY WTC-exposed firefighter cohort to incidence in the aforementioned NIOSH cohort, hereafter called the Career Firefighter Health Study (CFHS), and found no difference between the cohorts in the rate of all-cancers, although rates of some site-specific cancers were significantly elevated (e.g., thyroid and prostate cancer) in the FDNY cohort. Since post-9/11 follow-up in that study was limited to 8 years, and the latency period between exposure and most cancers is unknown, the current study extended follow-up to allow for the detection of cancers up to 15 years post-WTC exposure. We also utilized smoking data, when available, and we provide perspective for findings in firefighters (WTC-exposed and non-WTC-exposed) by comparing characteristics of these cases to those in the general population. This study is of importance to WTC research as it controls for both occupational exposures using a firefighter comparison group and US secular trends. The relationship between WTC exposure, firefighting and cancer is particularly worthy of close examination during this 20th anniversary year of the WTC attacks.

Methods

Study Population

Inclusion required that firefighters, both FDNY and CFHS, be actively employed by their respective departments on 11/9/2001. This study followed the STROBE guidelines and was approved by the Albert Einstein College of Medicine Institutional Review Board.

FDNY Cohort

The FDNY sample consisted of male firefighters who worked at the WTC site at any time between 11/9/2001-25/7/2002 (N=10,786). Male firefighters who did not report any WTC exposure (N=82) were excluded, as were WTC-exposed female firefighters (N=28) due to low numbers.

CFHS Cohort

The CFHS cohort included 29,992 firefighters from the Philadelphia, Chicago, and San Francisco Fire Departments, originally identified from department rosters, as previously described.[4, 21] We chose this referent group because they were subject to similar pre-hire fitness requirements, worked in urban environments, and worked at departments with retirement policies similar to FDNY's. Study inclusion was limited to males who were actively employed on 11/9/2001 (N=8,813); 585 females were excluded. All CFHS members are considered non-WTC-exposed.

Demographic/Background Information

Data were obtained from employee databases and FDNY medical records, and death information from the Social Security Death Master File and the National Death Index. One additional FDNY death was identified from employee records. Smoking status (current, former, or never smoker) was ascertained from health surveys completed by FDNY firefighters during medical monitoring examinations. A similar survey collected smoking and healthcare data from a sample of CFHS firefighters (Zeig-Owens et al., unpublished data, February 2021).

Cancer Cases

Information on cancer diagnoses was obtained by probabilistic matching to state cancer registries, as described elsewhere.[4, 19, 20] States were selected for linkage based on the residence information of active and retired FDNY and CFHS firefighters. The FDNY population was linked to Arizona, Connecticut, Florida, North Carolina, New Jersey, New York, Pennsylvania, South Carolina and Virginia state cancer registries. The CFHS population was linked to Arizona, California, Florida, Illinois, Indiana, Michigan, New Jersey, Oregon, Pennsylvania, and Washington state. Ninety-eight percent of FDNY firefighters and 97% of CFHS firefighters resided in one of the states selected for linkage. Only cancer cases defined as primary malignant tumors diagnosed between 11/9/2001 and 31/12/2016 were analyzed.

US Cancer Rates

We used the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (SEER-21) data to obtain rates of all-cancers and some site-specific cancers in the US male population.[22] Data were grouped by calendar year, race/ethnicity and 5-year age groups, and incidence rates calculated in these strata. We also obtained information on cancer stage at diagnosis[22] and median age at diagnosis.[23]

Statistical Analyses

Selected characteristics of each cohort were compared by calculating means (±SD), medians (IQR), or proportions (%), as appropriate. Follow-up time started on 11/9/2001 and ended on 31/12/2016 or, if earlier, date of death.

To examine trends over time, we graphed cancer incidence rates by calendar year in FDNY, CFHS and US males (SEER-21) using output from Poisson regression models of year and group predicting cancer cases, with the log of person-years as an offset, controlling for race/ethnicity and 5-year age group. To provide context for the interpretation of cancer risk in firefighters, with and without WTC exposure, our primary analyses involved estimating standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for all cancer sites combined (all-cancers) and some site-specific cancers[24] between 11/9/2001-31/12/2016, comparing each firefighter cohort with SEER-21. We used Poisson regression models with observed numbers of FDNY cancer cases as the outcome variable and the log of the expected case count in each demographic stratum, calculated by multiplying the stratum-specific SEER-21 rate with the number of person-years belonging to that stratum in the FDNY cohort, as an offset. We then re-ran these models using CFHS in place of FDNY data. Site-specific cancers were chosen based on our previous work examining post-9/11 cancer incidence in FDNY firefighters.[19, 20]

Additional primary analyses fit Poisson regression models assessing the associations between firefighter cohort and cancer rates, controlling for age on 9/11 and race/ethnicity. Adjusted relative rates (RRs) and 95% CIs were estimated

using cohort as the independent variable, cancer cases as the outcome, and log of person-years as the offset. The RR for melanoma was estimated from non-Hispanic white males (N=16,238) due to limited cases in non-whites.

Secondary analyses addressed possible surveillance bias, as previously described.[19, 20] Briefly, WTC-exposed FDNY firefighters undergo free health monitoring exams without co-pays, including blood testing, and chest CT scans, as indicated, even after retirement. FDNY cancers could therefore be diagnosed earlier due to screenings that are not widely available to others. Accordingly, we categorized cases of lung, liver, thyroid, or kidney cancer or Hodgkin or non-Hodgkin lymphoma diagnosed ≤6 months after chest CT scans and cases of prostate or hematological cancers diagnosed ≤6 months after routine blood tests as cases identified by screening (N=204), repeating the primary analyses after delaying the diagnosis dates of these cancers by two years.[20, 25]

Finally, we analyzed the subset of 10,723 FDNY and 2,856 CFHS firefighters for whom we had smoking information, re-doing the RR analyses comparing FDNY and CFHS cancer rates with smoking status (ever vs. never) included as a covariate in the models.

All analyses were performed in SAS (v9.4, SAS Institute Inc., Cary, NC, http://www.sas.com). Yearly incidence rate graphs were created via PROC SGPLOT using a locally weighted smoothing (LOESS) function for estimates generated from the first Poisson regression models described above.

Results

Selected characteristics of 10,786 WTC-exposed FDNY and 8,813 CFHS firefighters are shown in Table 1. FDNY firefighters were younger, and more likely to be white and never-smokers compared with CFHS firefighters. The FDNY cohort was also consistently younger at diagnosis compared with CFHS: for all-cancers (median [IQR]=55.6 [50.2-60.2] vs. 59.4 [54.4-64.8] years) and for every cancer subtype examined. Since 9/11, 92.7% of WTC-exposed male FDNY firefighters have had ≥1 PSA test, 98.8% ≥1 complete blood count, and 47.7% ≥1 chest CT. While we lack comparable data for the CFHS, 96% of those who completed the CFHS health survey reported a visit to a medical doctor within the previous two years.

Between 11/9/2001-31/12/2016, we identified 915 and 1,002 incident cancer cases in 841 FDNY and 909 CFHS firefighters, respectively. Prostate cancer was the most common site-specific cancer in both groups, followed by melanoma of the skin and non-Hodgkin lymphoma in FDNY, and lung cancer and melanoma in CFHS.

Cancer rates in firefighters (FDNY or CFHS) compared with US males (SEER-21)

Comparing median age at diagnosis across the three groups, we found that generally, FDNY firefighters had the youngest median age and SEER-21 the oldest.[23] Similarly, there were differences in cancer stage at diagnosis: FDNY firefighters were usually diagnosed at an earlier, more localized disease stage (Table 2).

Figure 1 displays the race/ethnicity- and age-group-adjusted cancer incidence rates by calendar year in the FDNY, CFHS and SEER-21 populations. Rates of prostate cancer (Figure 1A), non-Hodgkin lymphoma (Figure 1B) and melanoma of the skin (Figure 1C) were consistently elevated in the FDNY cohort compared with US males; this was especially evident for prostate cancer rates after 2007. Prostate cancer and melanoma rates also appeared to be elevated in CFHS vs. US males. In contrast, rates of lung cancer were *lower* in both firefighter cohorts than in US males (Figure 1D).

Table 3A displays results of SIR analyses comparing cancer incidence in the FDNY and CFHS cohorts with expected numbers based on SEER-21 rates. In the FDNY cohort, SIRs for all-cancers, prostate cancer, thyroid cancer, melanoma of the skin, and non-Hodgkin lymphoma were significantly elevated, whereas among CFHS firefighters prostate cancer and melanoma SIRs were significantly elevated. Lung cancer incidence was significantly *lower* than expectation in both cohorts.

After correction for possible surveillance bias, the FDNY all-cancer incidence remained modestly higher than expected compared with the US male population (SIR=1.09; 95% CI=1.02-1.16), as did the incidence of prostate, thyroid cancer and melanoma (Table 3B).

Cancer rates in FDNY compared with CFHS firefighters

Comparing the FDNY and CFHS cohorts directly, the FDNY cohort had significantly higher rates of all-cancer, prostate and thyroid cancer (Table 4). Race/ethnicity was generally not associated with cancer, although Black race was significantly associated with prostate cancer (RR=1.89, 95% CI=1.55-2.31). We also show results corrected for potential surveillance bias in the FDNY cohort: after correction, RRs were attenuated, but prostate and thyroid cancer rates remained significantly elevated in FDNY firefighters. In the analysis restricted to individuals for whom we had smoking information (N=13,579), the all-cancer RR was 15% higher in ever- vs. never-smokers, controlling for demographics and cohort membership (95% CI=1.02-1.30). Overall, >80% of lung cancer cases in this subpopulation (43/52) were reported in ever-smokers. After controlling for smoking status and demographics, FDNY members had higher rates of all-cancer and of prostate cancer compared with CFHS (RR=1.26, 95% CI=1.09-1.45 and RR=1.29, 95% CI=1.05-1.59, respectively.)

Discussion

On this, the 20th anniversary of 9/11, we set out to compare cancer rates in two firefighter cohorts, the WTC-exposed FDNY cohort and the non-WTC-exposed CFHS cohort, to each other and to rates among demographically similar men in the US population. No previous study of WTC-exposed rescue/recovery workers has assessed cancer risk using both an occupational comparison cohort and a general population. Further, no large study of cancers in firefighters has been able to incorporate smoking history into risk assessment.

We documented modest excesses of cancer risk in the WTC-exposed FDNY cohort in relation to each comparison group. First, comparing FDNY to the non-WTC exposed CFHS cohort, we found a 13% excess risk for all-cancers, largely driven by prostate and thyroid cancer. After correction for possible surveillance bias, excess risks were reduced, but not eliminated for prostate or thyroid cancer. Some proportion of the excess prostate cancer risk may be due to WTC exposure on top of usual firefighting risks, as some chemicals, like PCBs, commonly found at building sites including the WTC, are known endocrine disruptors, interfering with androgen metabolism.[26] This may have elevated the bioavailability of androgen, which could have been be a factor in prostate cancer initiation. For thyroid cancer, there is little biologic evidence for increased risk because radiation, the only clear environmental risk, was not detected at the WTC site. There is some evidence regarding thyroid cancer in pesticide-exposed workers;[27-29] pesticides, however, were also not reported at the site.[11-13] . Alternatively, high rates of some cancers, including thyroid and prostate cancers, could have resulted from non-biologic factors like enrollment in screening programs,[30] especially WTC-related health programs.[17-20, 31-33] Evidence for non-biologic factors due to screening include younger median age at diagnosis among the FDNY cohort for all-cancers and cancer subtypes compared with CFHS and SEER-21.[23] While the median ages at diagnosis were lowest for FDNY, CFHS median ages were also generally lower than SEER-21. Additional support for non-biologic factors can be found in the staging data: cancers reported in SEER-21 were less likely to be classified as localized at time of diagnosis, although data from SEER-21 contained more unknown stages than either FDNY or CFHS. Occupational and WTC-related health programs are designed for the early detection of cancer to minimize harm and improve survival. They clearly succeed in this mission, but may also over-diagnose occult, asymptomatic cancers (Goldfarb et al., unpublished data, February 2021).[17, 18]

Previous evidence from five non-WTC-exposed firefighter studies consistently supports excess risks of prostate cancer and melanoma in firefighters.[4, 8-10, 34] In our analyses, both firefighter cohorts had elevated rates of prostate cancer and melanoma relative to US males, although the SIRs for FDNY were higher. We proposed possible reasons for excess prostate cancer in firefighters above. As for melanoma, beyond UV exposure, melanoma has also been associated with PAH, PCB, aromatic hydrocarbons and other chemicals identified as present at the WTC[11, 13] and at non-WTC-related fires.[35]

Compared with US males, the FDNY cohort also had significantly elevated SIRs for all-cancer, non-Hodgkin lymphoma and thyroid cancer. The elevated all-cancer risk was driven by prostate cancer. After correcting for possible surveillance bias, we similarly observed elevated, albeit attenuated, SIRs. Despite our control efforts, surveillance bias concerns remain, as the US general population lacks access to comprehensive, no-copay healthcare like the WTC Health Program.[32]

The comparison group of CFHS firefighters is based on a subset of the original NIOSH cohort of 29,992 career firefighters.[4] Cancer data from the original cohort accrued from 1950-2009, whereas our study began and ended later, covering the time period between 9/2001-12/2016. Accordingly, some results from the full cohort are different from those we report. For example, compared with the US population, the earlier study found an all-cancer SIR of 1.09 (1.06-1.12)

and lung cancer SIR of 1.12 (1.04-1.21),[4] whereas we report SIRs of 1.05 (0.98-1.12) and 0.71 (0.57-0.89), respectively. We attribute these differences to our use of the truncated cohort (those active on 9/11). Notably, both firefighter groups had *lower* than expected rates of lung cancer when compared with US males, probably due to lower current smoking rates: 3.5%, 6.6% and 15.0% in the FDNY, CFHS, and US male populations, respectively.[36] Among firefighters with smoking data, ever-smokers demonstrated higher overall cancer rates than never-smokers. Differences in incident cancers may also be attributed to a previously described secular trend of declining cancer rates in firefighters hired since 1970, generally attributed to better PPE.[10]

Regular assessment of cancer risk in firefighters remains imperative because firefighting continues to be a common career and volunteer activity. Building contents (synthetics and plastics), fire suppression materials and PPE change over time and over geographic regions – facts which may explain inconsistent cancer results from previous studies.[3-10, 34] For example, The International Agency for Research on Cancer has classified perfluoroalkyl (PFA), a chemical used during suppression activities, as possibly carcinogenic to humans,[37] but has not yet fully evaluated this possibility. Differences in rates should also be considered in the context of behavioral changes (i.e., smoking; sunblock use) and in diagnostic testing (access; technology).

Finally, assessment of cancer risk in FDNY firefighters who worked at the WTC site remains complex; these firefighters were subject to carcinogenic exposures, while also enduring enormous physical and mental burdens related to the attacks. The current investigation extended our previous study, which used CFHS data to estimate excess risk in WTC-exposed FDNY firefighters through 31/12/2009.[20] Examination of longitudinal FDNY, CFHS and SEER-21 data by calendar year shows elevated cancer rates in the FDNY cohort, particularly prostate cancer between 2008-2012. While these increased rates may be driven by a greater number of FDNY retirees participating in medical monitoring after 2007, they could also reflect prostate cancer latency (Goldfarb et al., unpublished data, January 2021). Evidence is slowly accruing about cancer and other long latency illnesses in relation to WTC exposure, although much remains to be determined. Molecular epidemiologic studies of biomarkers may provide better understanding of chronic disease development in firefighters, both WTC-exposed and non-WTC-exposed.

Strengths of this study include the use of two different comparison groups to assess excess cancer risk in the WTC-exposed FDNY cohort, an achievement that no other group that we know of has been able to claim. Thus, we were able to report WTC-exposed firefighter cancer risk vs. risk in other firefighters and WTC-exposed risk vs. risk in demographically similar US males. In addition, we restricted analyses to firefighters actively employed on and after 9/11 not only to allow for WTC exposure comparison, but also so that findings would be relevant to firefighting in modern structures and PPE. Additional strengths include the lengthy follow-up time for each cohort (~15 years), and that smoking history was accounted for in those with available information.

Weaknesses include limitations common to all observational studies, that confounding may be insufficiently controlled in analyses, especially as we had more data from FDNY than from CFHS. For example, smoking history was available for nearly all FDNY firefighters and only 32% of CFHS. Also, we acknowledge that correction for surveillance bias by lagging FDNY diagnosis dates was an imperfect way to mitigate screening effects, as this lag time may be insufficient; in addition, asymptomatic cases in the US population, and to a lesser extent the CFHS cohort, may go undiagnosed without regular physical exams or adherence to screening programs. However, as cancer screening guidelines such as those from the United States Preventive Service Task Force[38] and the American Cancer Society[39] become more widely accepted, these differences should become less pronounced. For firefighters, these cancer screening guidelines have been recommended since 1997 by the International Association of Firefighters.[40] Although the fire departments in the CFHS cohort have had far less funding for cancer screening than FDNY, adjustment for surveillance bias only in the FDNY cohort could have led to an overestimation of this bias.

Clearer understanding of the WTC-related cancer risk for firefighters requires progress in at least two directions: additional years of follow-up to allow for the suspected long latency of some solid tumors; and, modeling studies (laboratory- or animal-based) to identify and track workplace exposures in WTC-exposed and non-WTC-exposed firefighters. These steps may aid our understanding of the complex relationships between WTC exposure, firefighting and cancer.

References

1. Campbell R, Evarts B. United States Firefighter Injuries in 2019. National Fire Protection Association; 2020.
2. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Painting, firefighting, and shiftwork. Lyon, France: IARC; 2010.

3. Bigert C, Martinsen JI, Gustavsson P, et al. Cancer incidence among Swedish firefighters: an extended follow-up of the NOCCA study. *International archives of occupational and environmental health*. 2020;93(2):197-204.
4. Daniels RD, Kubale TL, Yiin JH, et al. Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950-2009). *Occupational and environmental medicine*. 2014;71(6):388-97.
5. Glass DC, Pircher S, Del Monaco A, et al. Mortality and cancer incidence in a cohort of male paid Australian firefighters. *Occupational and environmental medicine*. 2016;73(11):761-71.
6. Harris MA, Kirkham TL, MacLeod JS, et al. Surveillance of cancer risks for firefighters, police, and armed forces among men in a Canadian census cohort. *American journal of industrial medicine*. 2018;61(10):815-23.
7. Kirstine Ugelvig Petersen K, Pedersen JE, Bonde JP, et al. Long-term follow-up for cancer incidence in a cohort of Danish firefighters. *Occupational and environmental medicine*. 2018;75(4):263-9.
8. LeMasters GK, Genaidy AM, Succop P, et al. Cancer risk among firefighters: a review and meta-analysis of 32 studies. *Journal of occupational and environmental medicine*. 2006;48(11):1189-202.
9. Pukkala E, Martinsen JI, Weiderpass E, et al. Cancer incidence among firefighters: 45 years of follow-up in five Nordic countries. *Occupational and environmental medicine*. 2014;71(6):398-404.
10. Casjens S, Brüning T, Taeger D. Cancer risks of firefighters: a systematic review and meta-analysis of secular trends and region-specific differences. *International archives of occupational and environmental health*. 2020;93(7):839-52.
11. Landrigan PJ, Lioy PJ, Thurston G, et al. Health and environmental consequences of the world trade center disaster. *Environmental health perspectives*. 2004;112(6):731-9.
12. Lioy PJ, Georgopoulos P. The anatomy of the exposures that occurred around the World Trade Center site: 9/11 and beyond. *Ann N Y Acad Sci*. 2006;1076:54-79.
13. Lioy PJ, Weisel CP, Millette JR, et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. *Environmental health perspectives*. 2002;110(7):703-14.
14. National Toxicology Program. NTP 12th Report on Carcinogens. *Report on carcinogens : carcinogen profiles*. 2011;12:iii-499.
15. Landgren O, Zeig-Owens R, Giricz O, et al. Multiple Myeloma and Its Precursor Disease Among Firefighters Exposed to the World Trade Center Disaster. *JAMA oncology*. 2018;4(6):821-7.
16. Li J, Brackbill RM, Liao TS, et al. Ten-year cancer incidence in rescue/recovery workers and civilians exposed to the September 11, 2001 terrorist attacks on the World Trade Center. *American journal of industrial medicine*. 2016;59(9):709-21.
17. Li J, Cone JE, Kahn AR, et al. Association between World Trade Center exposure and excess cancer risk. *Jama*. 2012;308(23):2479-88.
18. Solan S, Wallenstein S, Shapiro M, et al. Cancer incidence in world trade center rescue and recovery workers, 2001-2008. *Environmental health perspectives*. 2013;121(6):699-704.
19. Zeig-Owens R, Webber MP, Hall CB, et al. Early assessment of cancer outcomes in New York City firefighters after the 9/11 attacks: an observational cohort study. *Lancet (London, England)*. 2011;378(9794):898-905.
20. Moir W, Zeig-Owens R, Daniels RD, et al. Post-9/11 cancer incidence in World Trade Center-exposed New York City firefighters as compared to a pooled cohort of firefighters from San Francisco, Chicago and Philadelphia (9/11/2001-2009). *American journal of industrial medicine*. 2016;59(9):722-30.
21. Pinkerton L, Bertke SJ, Yiin J, et al. Mortality in a cohort of US firefighters from San Francisco, Chicago and Philadelphia: an update. *Occupational and environmental medicine*. 2020;77(2):84-93.
22. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 21 Regs Limited-Field Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2019 Sub (2000-2017) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2020, based on the November 2019 submission [Internet]. [Accessed 15 Oct 2020].
23. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975 - 2017, National Cancer Institute Based on November 2019 SEER data submission, April 2020. Available from: https://seer.cancer.gov/csr/1975_2017/ [Accessed 15 Jan 2021].

24. Surveillance, Epidemiology, and End Results Program. SEER Site Recode ICD-O-3/WHO 2008 Definition: National Cancer Institute; 2008. Available from: https://seer.cancer.gov/siterecode/icdo3_dwhoheme/index.html [Accessed 1 Oct 2020].
25. Andriole GL, Crawford ED, Grubb RLI, et al. Mortality Results from a Randomized Prostate-Cancer Screening Trial. *N Engl J Med*. 2009;360(13):1310-9.
26. Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, et al. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocrine reviews*. 2009;30(4):293-342.
27. Han MA, Kim JH, Song HS. Persistent organic pollutants, pesticides, and the risk of thyroid cancer: systematic review and meta-analysis. *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)*. 2019;28(4):344-9.
28. Lerro CC, Beane Freeman LE, DellaValle CT, et al. Pesticide exposure and incident thyroid cancer among male pesticide applicators in agricultural health study. *Environment international*. 2021;146:106187.
29. Zeng F, Lerro C, Lavoué J, et al. Occupational exposure to pesticides and other biocides and risk of thyroid cancer. *Occupational and environmental medicine*. 2017;74(7):502-10.
30. Patz EF, Jr., Pinsky P, Gatsonis C, et al. Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA internal medicine*. 2014;174(2):269-74.
31. Shapiro MZ, Wallenstein SR, Dasaro CR, et al. Cancer in General Responders Participating in World Trade Center Health Programs, 2003-2013. *JNCI cancer spectrum*. 2020;4(1):pkz090.
32. Colbeth HL, Genere N, Hall CB, et al. Evaluation of Medical Surveillance and Incidence of Post-September 11, 2001, Thyroid Cancer in World Trade Center-Exposed Firefighters and Emergency Medical Service Workers. *JAMA internal medicine*. 2020;180(6):888-95.
33. Yung J, Li J, Jordan HT, et al. Prevalence of and factors associated with mammography and prostate-specific antigen screening among World Trade Center Health Registry enrollees, 2015-2016. *Preventive medicine reports*. 2018;11:81-8.
34. Tsai RJ, Luckhaupt SE, Schumacher P, et al. Risk of cancer among firefighters in California, 1988-2007. *American journal of industrial medicine*. 2015;58(7):715-29.
35. Mehlman MA. Causal relationship from exposure to chemicals in oil refining and chemical industries and malignant melanoma. *Ann N Y Acad Sci*. 2006;1076:822-8.
36. Jamal A, King BA, Neff LJ, et al. Current Cigarette Smoking Among Adults - United States, 2005-2015. *MMWR Morbidity and mortality weekly report*. 2016;65(44):1205-11.
37. Agency for Toxic Substances and Disease Registry. ToxFAQs™ for Perfluoroalkyls. Available from: https://www.atsdr.cdc.gov/toxfaqs/tfacts200.pdf [Accessed 25 Jan 2021].
38. U.S. Preventive Services Task force. Recommendations. Available from: https://www.uspreventiveservicestaskforce.org/uspstf/topic_search_results?category%5B%5D=15&searchterm=Cancer [Accessed 6 Feb 2021].
39. American Cancer Society. American Cancer Society Guidelines for the Early Detection of Cancer. Available from: https://www.cancer.org/healthy/find-cancer-early/cancer-screening-guidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html [Accessed 6 Feb 2021].
40. International Association of Fire Fighters. The Fire Service Joint Labor Management Wellness-Fitness Initiative. 4th ed. 2018.

Table 1: Population Characteristics

	WTC-exposed male FDNY firefighters active on 9/11	**Male CFHS firefighters actively employed on 9/11**
Total N	10,786	8,813
Age on 9/11, mean ± SD	40.4±7.5	43.9±9.2

Race/ethnicity, N (%)		
White	10,121 (93.8)	6,117 (69.4)
Black	282 (2.6)	1,589 (18.0)
Hispanic	353 (3.3)	736 (8.3)
Other[a]	30 (0.3)	371 (4.2)
Smoking status, N (%)		
Current	373 (3.5)[b]	189 (6.6)[c]
Former	3,233 (30.2)[b]	1,056 (37.0)[c]
Never	7,117 (66.4)[b]	1,611 (56.4)[c]
Age at cancer diagnosis, median (IQR)		
All cancers	55.6 (50.2-60.2)	59.4 (54.4-64.8)
Prostate cancer	57.9 (53.3-62.4)	60.4 (55.2-65.4)
Lung cancer	60.4 (55.6-65.5)	62.8 (57.9-67.2)
Kidney cancer	56.0 (49.0-63.0)	58.1 (54.7-63.2)
Non-Hodgkin lymphoma	53.6 (48.9-59.4)	60.1 (50.1-65.3)
Melanoma (skin)	51.9 (45.5-57.8)	61.2 (54.4-66.5)
Thyroid cancer	51.2 (44.0-56.5)	59.0 (49.2-64.5)
Alive at end of follow-up, N (%)	10,525 (97.6)	8,208 (93.1)
Follow-up time (years), mean ± SD	15.2 ± 1.1	14.9 ± 2.0

[a]Includes Asian and Native American race categories; [b]N=10,723 who self-reported smoking status; [c]N=2,856 who completed CFHS survey

Table 2: Proportion of cancers[a] in localized, regional, distant, or unknown stage at time of diagnosis (%)

Site		FDNY[b]	CFHS[c]	SEER-21[d]
Prostate	Localized	78.9	77.7	62.0
	Regional	11.7	14.0	9.0
	Distant	2.1	1.7	4.0
	Unknown	7.2	6.7	24.0
Lung	Localized	45.5	15.7	14.2
	Regional	20.5	26.5	18.0
	Distant	29.6	51.8	43.5
	Unknown	4.5	6.0	24.4
Kidney	Localized	79.5	67.3	55.3
	Regional	17.9	12.7	14.3
	Distant	2.6	16.4	12.7
	Unknown	0	3.6	17.7
Non-Hodgkin Lymphoma	Localized	32.7	32.6	22.3
	Regional	9.1	13.9	12.0
	Distant	49.1	41.9	41.9
	Unknown	9.1	11.6	23.7
Melanoma (skin)	Localized	71.2	78.6	68.5
	Regional	4.2	2.9	8.0
	Distant	4.2	7.1	4.1
	Unknown	19.8	11.4	19.3

Thyroid	Localized	65.2	53.3	51.6
	Regional	32.6	16.7	28.8
	Distant	0	0	5.7
	Unknown	2.2	0	13.8

[a]All malignant cancers (multiple primaries);
[b]Fire Department of the City of New York; [c]Career Firefighter Health Study;
[d]Surveillance, Epidemiology, and End Results Program[22]

Table 3a: Standardized Incidence Ratios (SIRs) of cancers in male FDNY[a] and CFHS[b] firefighters vs. US males,[22] 11/9/2001-31/12/2016

Site	FDNY[a] SIR	95% CI	CFHS[b] SIR	95% CI
All cancer sites[c]	1.15	(1.08-1.23)	1.05	(0.98-1.12)
Prostate	1.70	(1.53-1.88)	1.22	(1.11-1.35)
Lung	0.53	(0.39-0.72)	0.71	(0.57-0.89)
Kidney	0.93	(0.67-1.28)	1.19	(0.90-1.56)
Non-Hodgkin Lymphoma	1.39	(1.06-1.83)	1.04	(0.77-1.41)
Melanoma (skin)	1.59	(1.30-1.96)	1.39	(1.07-1.79)
Thyroid	2.37	(1.78-3.17)	1.01	(0.61-1.67)

[a]Fire Department of the City of New York; [b]Career Firefighter Health Study;
[c]All malignant cancers (multiple primaries), and in situ bladder cancers

Table 3b: Standardized Incidence Ratios (SIRs) of cancers in male FDNY[a] firefighters vs. US males,[22] 11/9/2001-31/12/2016, after adjustment for potential surveillance bias

Site	SIR[c]	95% CI
All cancer sites[b]	1.09	1.02-1.16
Prostate	1.55	1.39-1.73
Lung	0.47	0.34-0.65
Kidney	0.85	0.61-1.19
Non-Hodgkin Lymphoma	1.29	0.97-1.71
Melanoma (skin)	1.59	1.30-1.96
Thyroid	2.01	1.47-2.75

[a]Fire Department of the City of New York;
[b]All malignant cancers (multiple primaries), and in situ bladder cancers
[c]Diagnosis dates of certain FDNY cancer cases (N=204) delayed by 2 years to account for potential surveillance bias

Table 4: Adjusted relative rates (RR) and surveillance bias-adjusted RR of cancers in WTC[a]-exposed male FDNY[b] firefighters vs. male CFHS[c] firefighters, 11/9/2001-31/12/2016

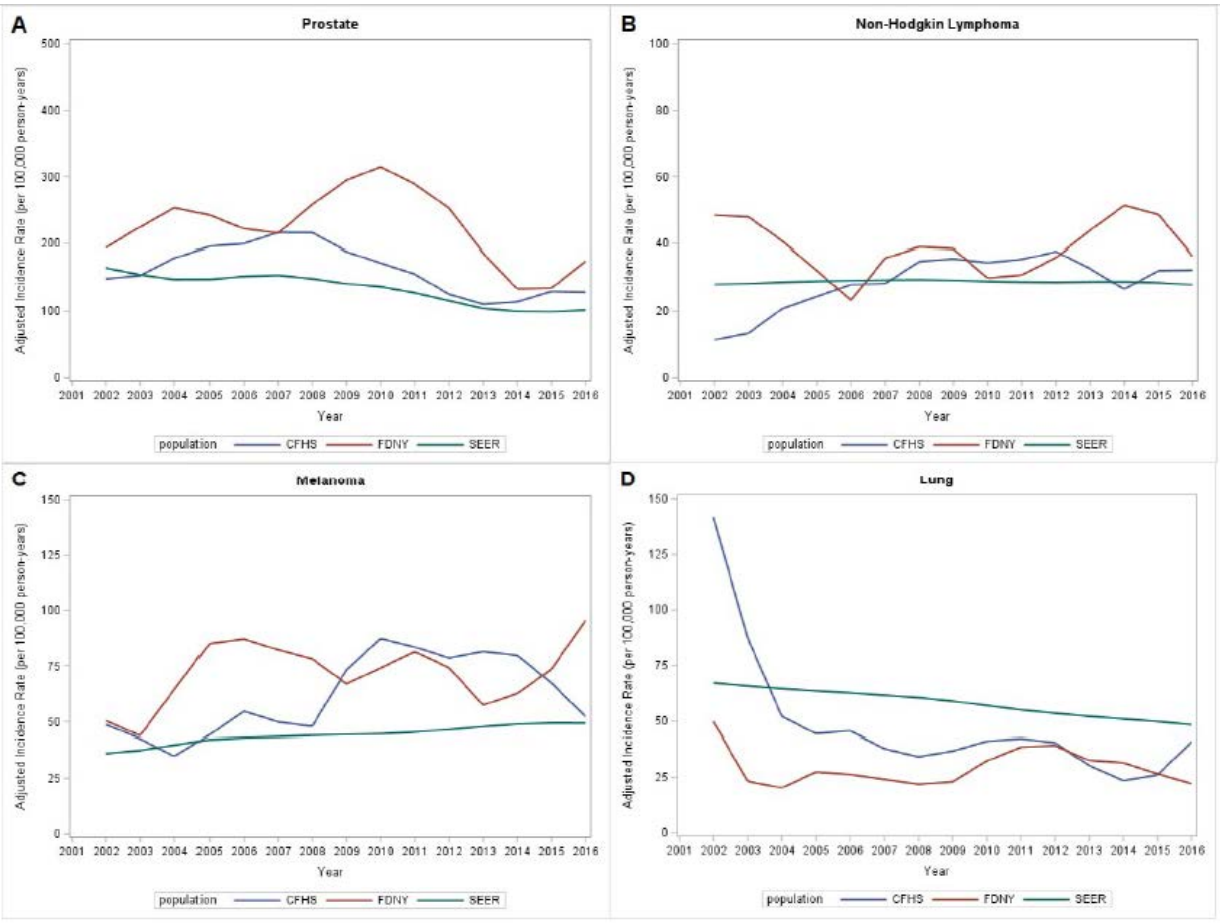
Site	Adj. RR (95% CI)[f]	Surveillance Bias Adj. RR (95% CI)[fg]
All cancer sites[d]	1.13 (1.02-1.25)	1.07 (0.96-1.18)

Prostate	1.39 (1.19-1.63)	1.28 (1.09-1.51)
Lung	0.87 (0.57-1.33)	0.77 (0.50-1.19)
Kidney	0.82 (0.52-1.30)	0.75 (0.47-1.20)
Non-Hodgkin Lymphoma	1.26 (0.80-2.00)	1.21 (0.75-1.94)
Melanoma (skin)[ef]	1.12 (0.80-1.57)	N/A
Thyroid	2.53 (1.37-4.70)	2.11 (1.14-3.90)

[a]World Trade Center; [b]Fire Department of the City of New York; [c]Career Firefighter Health Study;
[d]All malignant cancers (multiple primaries), and in situ bladder cancers;
[e]Analysis restricted to white males (N=16,238) due to low case counts in other race/ethnic groups;
[f]Regression models adjusted for age on 9/11/2001 and race/ethnicity;
[g]Diagnosis dates of some FDNY cancer cases (N=204) delayed by 2 years to account for potential surveillance bias.

Figure Legend

Figure 1. Incidence of site-specific cancers by calendar year in World Trade Center (WTC)-exposed firefighters, non-WTC-exposed firefighters, and US males. Shown are the adjusted incidence rates over time of selected site-specific cancers, estimated by applying a locally weighted smoothing function to output from Poisson regression models of calendar year and cohort predicting cancer cases. **Panel A** shows estimated incidence rates of prostate cancer by calendar year in WTC-exposed Fire Department of the City of New York (red) and non-WTC-exposed Career Firefighter Health Study male firefighters (blue) vs. in US males based on Surveillance, Epidemiology, and End Results Program data (green). **Panels B, C and D** show estimated yearly incidence rates for non-Hodgkin lymphoma, melanoma, and lung cancer, respectively, in the above three populations. Rates were adjusted for race/ethnicity and 5-year age group.


A
Prostate
Adjusted Incidence Rate (per 100,000 person-years)
Year
population CFHS FDNY SEER
B
Non-Hodgkin Lymphoma
Adjusted Incidence Rate (per 100,000 person-years)
Year
population CFHS FDNY SEER
C
Melanoma
Adjusted Incidence Rate (per 100,000 person-years)
Year
population CFHS FDNY SEER
D
Lung
Adjusted Incidence Rate (per 100,000 person-years)
Year
population CFHS FDNY SEER

Aim 2

Establish a well-characterized cohort of firefighters from the Firefighter Comparison Cohort for lifelong follow-up.

Assembling the Career Firefighter Health Study Cohort: A Methods Overview

Rachel Zeig-Owens, DrPH, MPH, Ankura Singh, MPH, Suzanne Triplett, BA, Joke Salako, MPH, Molly Skerker, MPH, Ariana Napier, MA, BA, Eric Peele, BA, Marshica Stanley, MA, BS, Sridevi Sattaluri, MS, BS[3], David Prezant, MD and Mayris P. Webber, DrPH, MPH

Introduction

The attacks on the World Trade Center (WTC) on September 11, 2001 (9/11) exposed rescue/recovery workers as well as area residents and others to vast quantities of dust, smoke, and toxins as a result of the combustion of jet fuel and the collapse of the WTC Towers. The pulverized cement, glass, and building contents generated thousands of tons of particulate matter, components of which included asbestos, lead, polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), organochlorine pesticides, and polychlorinated furans and dioxins.[1,2]

Hundreds of studies of WTC-exposed rescue/recovery workers and others have been published in the peer-reviewed literature. Many of these studies report the incidence and prevalence of conditions and symptoms that are thought to occur more commonly as consequences of exposure to the WTC disaster site. To date, studies have shown that WTC exposures, particularly among rescue/recovery workers, are associated with aerodigestive conditions (i.e., obstructive airways disease, chronic rhinosinusitis and gastroesophageal reflux disease), mental health conditions (i.e., posttraumatic stress disorder and depression) and cancer.[3-12] However, the extent to which these associations are due to WTC exposure versus other occupational exposures or to unrelated factors is still under investigation because rates of these conditions in suitable comparison groups are generally unavailable.

One of the largest groups of WTC-exposed rescue/recovery workers is made up of firefighters from the Fire Department of the City of New York (FDNY). Firefighting has been associated with cancer and other health risks, such as asthma, because of the potential for inhalation and contact exposures to harmful substances.[13-22] Thus, firefighting exposures outside of work at the WTC site may confound studies of the association between WTC exposure and disease outcomes in WTC-exposed firefighters. Conversely, hiring standards for firefighters require that applicants meet stringent health criteria. This results in a physically superior workforce which may more easily withstand the effects of noxious exposures and as such, results may also be impacted by the healthy worker effect.[23]

To assess the health effects of WTC-related rescue/recovery work versus effects associated with non-WTC-related firefighting, a comparison cohort of firefighters from Chicago, Philadelphia and San Francisco who did not respond to the WTC attacks was identified. This firefighter cohort was originally assembled by the National Institute for Occupational Safety and Health (NIOSH) for their multi-year study (1950-2009) of nearly 30,000 professional firefighters in order to assess the potential link between firefighting and cancer. We re-named the original NIOSH cohort the “Career Firefighter Health Study” cohort. This comparison cohort is important because, as stated, firefighting exposures outside of WTC work may confound studies of the association between WTC-exposure and disease outcomes in WTC-exposed firefighters, and non-FDNY firefighters have similar pre-hire health requirements. Further, although population-based comparisons may be available for cancer (e.g., Surveillance, Epidemiology, and End Results Program [SEER]), mortality (National Death Index [NDI]), and occasionally for other diagnoses, external comparison populations present issues of comparability,[24] as the general population may differ from the occupational group in the prevalence of pre-existing health conditions (e.g., heart disease) that interfere with their ability to work. Finally, maintenance of a non-WTC-exposed cohort will permit estimates of the incidence of adult-onset conditions like asthma, which are currently lacking. In future studies, the Career Firefighter Health Study cohort will be combined with non-WTC-exposed FDNY firefighters to give a broader picture of the health status of US firefighters.

The Career Firefighter Health Study cohort will be used for two primary purposes for WTC-related research: it serves as a non-WTC-exposed comparison population for cancer research via linkages to state cancer registry data. Secondly, it also serves as a non-WTC exposed comparison population for assessment of chronic physical and mental health conditions via health surveys.

To be able to compare rates of cancer in the WTC-exposed FDNY firefighter cohort to rates in the non-WTC exposed Career Firefighter Health Study cohort, we performed linkages with various state cancer registries, as previously described.[12,14,25] In this methodological report, we present only a brief overview of the time interval between initial submission of 10 applications to state cancer registries to final acquisition of data. The primary focus of the current account is to document the processes used for the identification and follow-up of firefighters from the Career Firefighter Health Study cohort, and to detail the efforts required for their engagement and participation in the baseline health survey. Most of the follow-up outreach was performed in collaboration with our partners, RTI International, a non-profit research institute that we hired for contact tracing, although these efforts were overseen and coordinated by the principal investigator and co-investigators from Montefiore Medical Center/Albert Einstein College of Medicine.

Materials and Methods

Career Firefighter Health Study population

The source population provided by NIOSH was established from roster information supplied by the Chicago, Philadelphia and San Francisco Fire Departments.[14] All Career Firefighter Health Study firefighters were employed by their respective departments for at least 1 day between 1/1/1950 and 12/31/2009 (n=29,992).

Recruitment for the baseline health survey was restricted to the subset of the cohort not known to be deceased at initiation of follow-up in February 2019 (n=14,566 or 48.6%), based on vital status tracing, as outlined below. The Career Firefighter Health Study was endorsed by both management and unions from FDNY, the Chicago Fire Department, the Philadelphia Fire Department and the San Francisco Fire Department, as well as by the International Association of Fire Fighters (IAFF). This study was approved by the Institutional Review Boards at Albert Einstein College of Medicine/Montefiore Medical Center and RTI International and informed consent was obtained for the surveys.

Career Firefighter Health Study Master File and Tracing

For cancer analyses, initial IRB approvals and data use agreements (DUAs) with NIOSH, each fire department, and RTI International allowed for the Career Firefighter Health Study cohort of 29,992 firefighters to be sent to state cancer registries, and so we obtained the fire department roster information for the full cohort. NIOSH provided a master file containing first name, last name, social security number (SSN), sex, race, fire department (Chicago, Philadelphia or San Francisco), and dates of birth, hire and retirement (if applicable) for 29,992 individuals. Full SSN was available for 93% of the cohort (Table I). Additionally, address information including street address, city, state and zip code was included when available.

To identify the subset of individuals who were alive and therefore potentially available for follow-up, hereafter referred to as the Career Firefighter Health Study Outreach Cohort, RTI conducted vital status tracing, limited to cohort members who were actively employed on or after 1/1/1987 (N=17,464) to both limit expenses and improve the likelihood of current identification (Figure 1). Accordingly, this subset of the population was linked to the Centers for Disease Control and Prevention's National Death Index (NDI) for vital status as well as cause of death data through 12/31/2016. We also submitted individuals' information to the Social Security Administration Limited Access Death Master File (SSA-LADMF), which had more recent vital status data available, although it is estimated to be missing some deaths and does not include cause of death information.

Tracing Activities for Follow-Up

Once the Career Firefighter Health Study Outreach Cohort was identified by NDI and SSA-LADMF matches (N=14,566), RTI conducted batch tracing at two timepoints using specialized vendors to update home addresses and obtain recent telephone numbers and e-mail addresses. This automated process reduced the number of individuals requiring manual locating during data collection. Of those not known to be deceased, 98% were found via these tracings, resulting in new or additional contact information. Tracing was continuously updated throughout the data collection period for individuals whose contact information was inaccurate, such as a phone number returning a disconnected signal. These expanded efforts included manually searching a portfolio of proprietary search engine databases and credit bureaus for contact information. Through these manual efforts, additional contact information was obtained for 759 firefighters.

Career Firefighter Health Study Survey

We developed the web-based survey instrument for the Career Firefighter Health Study based on surveys regularly completed by FDNY firefighters during routine medical monitoring visits, since October 2001.[26-28] The survey covers demographic information as well as important health topics that affect firefighters' health and safety, such as

physical and mental health symptoms and doctor diagnoses, work exposures, and tobacco and alcohol use.[29-31] The development process involved reviewing the FDNY survey and identifying questions that needed to be included for comparability to information available for the FDNY cohort, which, in addition to survey data, incorporates information from employment sources (e.g., race) or verified diagnoses and dates with medical records. The additional questions were added by adapting questions from reliable sources such as the National Health and Nutrition Examination Survey and then showing the questions to a group of FDNY firefighters for input. Lastly, we modified response options to limit acceptable responses to specific ranges and included "Don't know" so a participant could continue the survey despite unknown or private information.

Once the questions were finalized, the FDNY Bureau of Technology Development and Systems programmed the survey to be taken on the internet using either a computer or tablet. Initially, the surveys were checked in the testing environment so that data files could be output and reviewed to identify and resolve problems with range checks, skip logic, and missing data. Then the survey was deployed into production on the secure FDNY Cloud which is run on the Oracle Cloud platform. Additionally, an application programming interface (API) - computing interface which defines interactions between multiple software intermediaries - was developed so that an RTI-staffed call center could process data for reports for outreach calls. Trained CFHS interviewers and supervisors worked at RTI Research Operations Center and conducted phone interviews with participants who preferred this modality. Once a participant completed the survey, a process was put in place to send a $10 Amazon eGift Card to the email address provided during the survey. If a participant requested a $10-cash card instead, the system was programmed to alert the research staff of this choice. It took 10 months to fully program the survey and deploy it to production on the study website.

Recruitment and outreach

After batch tracing was complete, we began contact activities; these included sending all participants multiple letters and postcards explaining the study goals, describing endorsements by local and national fire officials, and inviting them to participate by completing the survey. Recruitment was staggered in order to focus energy and effort on one city fire department at a time: San Francisco was the first beginning 2/12/2019, Philadelphia the second beginning 5/8/2019, and Chicago the final study site beginning 10/21/2019. All sites were recruited following a similar strategy. The first invitation letter was sent in collaboration with each fire department and the local unions -- firefighters from San Francisco received a letter signed by the San Francisco Chief of Department and the San Francisco Firefighters Union Local 798 President. Firefighters from Philadelphia received a letter signed by the Philadelphia Fire Commissioner and the Philadelphia Firefighters and Paramedics' Union IAFF 22 President. Firefighters from Chicago received a letter signed by the Chicago Fire Commissioner and the Chicago Firefighters Union Local 2 Vice President. Members of the city fire departments and the President of International Association of Fire Fighters (IAFF) each recorded short promotional videos for the study. A link to these videos was provided in all communication. In addition, email invitations were sent to those participants who had an email address obtained through batch tracing. All methods of communication included information on the purpose of the Career Firefighter Health Study, credentials to complete the survey via the internet, and a toll-free number for questions and for survey completion by telephone, if desired. To promote the study effectively, we regularly consulted each fire department and tailored our messages to appeal to as broad a population of firefighters as possible. For example, all printed materials included photographs specific to each fire department. Outreach began for each city once the invitation letter was approved by each city fire department and local union. The number of attempts differed by city based on communication with the individual fire departments and response rates.

In addition to mail and email contacting activities, RTI conducted outreach telephone calls to non-respondents. Ten telephone interviewers and four supervisors assigned to this project were trained on the study background, confidentiality and informed consent requirements, refusal avoidance techniques, and quality control and performance expectations. We developed a comprehensive training manual for phone interviewers to refer to during the project. As part of their training, they had to complete at least 2 practice interviews and accurately explain the purpose and goals of the study and provide technical assistance for lost password information. Before placing a prompting call to a study participant, interviewers reviewed case notes for each case. If the interviewer reached the participant's voicemail, a project-approved message was left on the voicemail. Algorithms were programmed to prompt interviewers when and if to leave a message for each person. The call center system also had callback delays programmed so that the cases were not contacted too close to or distant from previous attempts.

Quality Control and Management

To facilitate collaboration with RTI, we established weekly phone calls and/or emails with the study team to discuss the progress of the study. Once data collection started, we actively monitored production levels, including a daily report of the distribution of cases who started the survey, completed the survey and refused the survey. RTI also submitted weekly progress reports to keep FDNY apprised of the project's status regarding work accomplished. Reports provided an overview of tracing and data collection progress completed during the week and noted any anticipated problems or concerns.

Statistical Analyses

We calculated proportions (%), means (±SD) or medians (IQR) to assess survey responses and demographic characteristics, as appropriate. The chi-squared test evaluated differences between the demographics of Career Firefighter Health Study survey respondents and non-respondents, and between the full Career Firefighter Health Study Outreach Cohort and the FDNY WTC-exposed firefighter population (N=13,317). All data analyses were performed in SAS (version 9.4, SAS Institute Inc., Cary, NC).

Results

Cancer Linkage Results

Cancer outcomes were obtained via linkages with 10 state cancer registries. The methods for linkages were standard, but the time interval between submission of IRB applications to the state cancer registries and final acquisition of data varied greatly. Dates of state cancer registry IRB submissions ranged from 8/8/2017 to 1/10/2019, as the latest submission date was caused by a state that was unable to accept applications for ~18 months. Formal IRB approvals were received from 9/21/2017 to 7/16/2019. We received the linked cancer datafiles between 7/12/2019 and 6/12/2020. After the removal of identical cancer cases received from more than one state, we identified 6,260 unique cases for the full Career Firefighter Health Study cohort of 29,992.

Career Firefighter Health Study Survey

Of the 29,992 individuals provided in the master file from NIOSH, a total of 12,528 were classified as not contactable, and 2,898 classified as deceased after linkages to NDI and SSA-LADMF. A flowchart detailing the results from these linkages is presented as Figure 1. All 14,566 individuals not known to be deceased were included in the Career Firefighter Health Study Outreach Cohort and eligible for survey data collection. The Career Firefighter Health Study Outreach Cohort had a greater proportion of older adults, females and nonwhites than the FDNY cohort of WTC-exposed firefighters (Table II).

A total of 4,962 participants responded to the baseline survey between 2/15/2019 and 12/15/2020 for an overall rate of 34.1%. The response rates varied by site, with San Francisco having the highest rate. The response rates by site were 43.1% (N=1,163), 34.5% (N=1,442) and 30.7% (N=2,357) for San Francisco, Philadelphia and Chicago, respectively. Postcard mailings produced the highest response rate compared with letters or email reminders: reminder postcards resulted in an average (±SD) of 40.2 ±47.7, 44.4 ±28.4 and 63.2 ±34.2 responses within one week following each postcard mailing in the San Francisco, Philadelphia and Chicago groups, respectively. All participants who completed any survey questions in addition to the consent form at the start of the survey were counted as respondents for the purpose of calculating response rates. The response rates, including refusals by site, are described below (Table III). The most common reasons for refusal were disinterest in the study and being too busy to participate. Approximately, 98% of those who completed the survey elected to receive their incentive via email, whereas 2% of respondents asked for an alternate option. Most participants (90%) completed the survey via the internet (Table III). Firefighters median time to complete the survey was 35 minutes (IQR: 26.1-48.9), which was within the expected range.

We examined the demographic information of respondents and non-respondents (Table IV). The respondent and non-respondent groups had similar proportions of males and females. Respondents were older than non-respondents, however, and more likely to identify as non-Hispanic white.

Discussion

Firefighting is a dangerous profession that has the potential for both short- and long-term health consequences, such as cancer and respiratory diseases.[13-22] Firefighters exposed to the WTC disaster may have substantially greater risks of these and other health conditions.[12,25] Disentangling routine firefighting exposures from the complex exposures present at the WTC site is challenging. The Career Firefighter Health Study cohort provides a suitable comparison population for WTC-exposed firefighters so that health outcomes in WTC disaster-exposed workers can be evaluated, independent of

firefighting exposures. Here we detail some of the steps and challenges in identification and recruitment of a suitable comparison population.

One of the main objectives of our study was to compare cancer risk in the WTC-exposed FDNY cohort to risk in other urban firefighters, namely, those in the Career Firefighter Health Study cohort. To do this, we obtained IRB approvals from 10 state cancer registries and linked the Career Firefighter Health Study cohort to each. However, the time interval between submission of state registry IRB applications and receipt of data was longer than we anticipated: it took 34 months or nearly three years to obtain cancer data from all 10 states. This process was also complicated in part due to changes in key personnel (both legal and administrative) in the local Fire Departments and in the union management in the years since the original cohort was first assembled. Our intention was for this manuscript to provide valuable information on the procedures and processes that might be used in future studies of firefighters or other occupational populations for long-term follow up. Some of our findings point to areas for improvement in response rates, contacting protocols, instrumentation and analysis. These lessons learned and their implications are detailed in the sections below.

The biggest challenge for all studies of this type, including our own, was the survey response rate; our survey response rate was lower than we had hoped. Approximately one third of the 14,566 individuals eligible for data collection responded to the survey, primarily via the web-based version (~90% of respondents). While one third of the eligible population is a proportion consistent with published data on survey response rates in epidemiological studies,[32,33] the response rate was likely impacted by several factors.

First, and most importantly, there were challenges with contacting firefighters and updating contact information. The original sample file included data from firefighters followed through 2009, which was nearly a decade before we initiated contact tracing. Additionally, while over three quarters of the cohort had an address in the original sample file, much of the data were out-of-date, which made it hard to know if non-respondents received the mailings, telephone prompting calls or emails. To increase the number of respondents, several steps were taken. The data collection period was extended, and more experienced personnel were trained to trace and conduct interviews. We also monitored response rates and found that postcard mailings produced the highest rate compared with letters or emails. Therefore, we sent out additional postcard mailings when it became clear that the number of final completed interviews was going to be lower than expected. For future investigators attempting outreach in a demographically similar population, we would therefore emphasize the importance of obtaining current mailing addresses via batch tracing; mailing address may be the most reliable form of contact information for a source population consisting primarily of middle-aged and older men. In addition, we contacted members of the individual fire departments and/or unions to discuss other outreach options (e.g., putting an ad in the union newsletter). These measures increased the absolute number of completed surveys but did not substantially change response rates. Finally, our response rate may have become depressed, especially in Chicago, due to the coronavirus disease 2019 (COVID-19) pandemic. Other national surveys have observed a similar impact in response rates during this period.[34]

Lower response rates impact both sample size and study generalizability.[35] As shown in Table IV, those who responded to the survey were slightly older and whiter than the eligible population. Given this, we plan to continue to reach out to the fire departments and local unions as well as establish relationships with firefighting fraternities (e.g., African American Firefighter and Paramedic League and the Vulcan Society) that represent the subgroups with lower response rates.

The Career Firefighter Health Study survey is the first to collect information on chronic physical and mental health conditions among US firefighters. The data collected from nearly 5,000 survey respondents will inform WTC-related research as well as general firefighting research. For the cancer comparison analyses, we obtained additional years of cancer data for the full Career Firefighter Health Study cohort of 29,992 firefighters through linkages with state cancer registries, and now have IRB protocols in place which enable us to continue matching at 5-year intervals. The survey and cancer data will have an important impact on studies of WTC rescue/recovery work, firefighting and related health conditions. First, as a comparison population to the FDNY WTC-exposed firefighters, it will be used to determine the extent to which the observed association between WTC exposure and chronic physical and mental health conditions among WTC-exposed firefighters may be confounded by firefighting exposures. Additionally, we have expanded on the scope of the original study of firefighting and cancer conducted by Daniels et al. by collecting self-reported health outcomes as well as important health covariates such as smoking history. Lastly, we have established a cohort that will be followed longitudinally to assess the health impact of firefighting over time, especially if we can replenish the Career Firefighter Health Study Cohort with members who joined these fire departments after 2009.

References

1. Lioy PJ, Weisel CP, Millette JR, et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. *Environmental health perspectives.* 2002;110(7):703-714.
2. McGee JK, Chen LC, Cohen MD, et al. Chemical analysis of World Trade Center fine particulate matter for use in toxicologic assessment. *Environmental health perspectives.* 2003;111(7):972-980.
3. Hall CB, Liu X, Zeig-Owens R, et al. The Duration of an Exposure Response Gradient between Incident Obstructive Airways Disease and Work at the World Trade Center Site: 2001-2011. *PLoS Curr.* 2015;7.
4. Li J, Cone JE, Kahn AR, et al. Association between World Trade Center exposure and excess cancer risk. *Jama.* 2012;308(23):2479-2488.
5. Liu C, Putman B, Singh A, et al. Abnormalities on Chest Computed Tomography and Lung Function Following an Intense Dust Exposure: A 17-Year Longitudinal Study. *Int J Environ Res Public Health.* 2019;16(9):1655.
6. Liu X, Yip J, Zeig-Owens R, et al. The Effect of World Trade Center Exposure on the Timing of Diagnoses of Obstructive Airway Disease, Chronic Rhinosinusitis, and Gastroesophageal Reflux Disease. *Front Public Health.* 2017;5:2-2.
7. Prezant DJ, Weiden M, Banauch GI, et al. Cough and bronchial responsiveness in firefighters at the World Trade Center site. *The New England journal of medicine.* 2002;347(11):806-815.
8. Solan S, Wallenstein S, Shapiro M, et al. Cancer incidence in world trade center rescue and recovery workers, 2001-2008. *Environmental health perspectives.* 2013;121(6):699-704.
9. Soo J, Webber MP, Gustave J, et al. Trends in probable PTSD in firefighters exposed to the World Trade Center disaster, 2001-2010. *Disaster medicine and public health preparedness.* 2011;5 Suppl 2:S197-203.
10. Weakley J, Webber MP, Gustave J, et al. Trends in respiratory diagnoses and symptoms of firefighters exposed to the World Trade Center disaster: 2005-2010. *Prev Med.* 2011;53(6):364-369.
11. Wisnivesky JP, Teitelbaum SL, Todd AC, et al. Persistence of multiple illnesses in World Trade Center rescue and recovery workers: a cohort study. *Lancet.* 2011;378(9794):888-897.
12. Zeig-Owens R, Webber MP, Hall CB, et al. Early assessment of cancer outcomes in New York City firefighters after the 9/11 attacks: an observational cohort study. *Lancet.* 2011;378(9794):898-905.
13. Bigert C, Martinsen JI, Gustavsson P, Sparén P. Cancer incidence among Swedish firefighters: an extended follow-up of the NOCCA study. *International archives of occupational and environmental health.* 2020;93(2):197-204.
14. Daniels RD, Kubale TL, Yiin JH, et al. Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950-2009). *Occupational and environmental medicine.* 2014;71(6):388-397.
15. Glass DC, Pircher S, Del Monaco A, Hoorn SV, Sim MR. Mortality and cancer incidence in a cohort of male paid Australian firefighters. *Occupational and environmental medicine.* 2016;73(11):761-771.
16. Harris MA, Kirkham TL, MacLeod JS, Tjepkema M, Peters PA, Demers PA. Surveillance of cancer risks for firefighters, police, and armed forces among men in a Canadian census cohort. *Am J Ind Med.* 2018;61(10):815-823.
17. International Agency for Research on Cancer. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Painting, firefighting, and shiftwork.* Vol 98. Lyon, France: IARC; 2010.
18. Kirstine Ugelvig Petersen K, Pedersen JE, Bonde JP, Ebbehoej NE, Hansen J. Long-term follow-up for cancer incidence in a cohort of Danish firefighters. *Occupational and environmental medicine.* 2018;75(4):263-269.
19. LeMasters GK, Genaidy AM, Succop P, et al. Cancer risk among firefighters: a review and meta-analysis of 32 studies. *Journal of occupational and environmental medicine.* 2006;48(11):1189-1202.
20. Pedersen JE, Ugelvig Petersen K, Ebbehøj NE, Bonde JP, Hansen J. Risk of asthma and chronic obstructive pulmonary disease in a large historical cohort of Danish firefighters. *Occupational and environmental medicine.* 2018;75(12):871-876.
21. Pukkala E, Martinsen JI, Weiderpass E, et al. Cancer incidence among firefighters: 45 years of follow-up in five Nordic countries. *Occupational and environmental medicine.* 2014;71(6):398-404.
22. Ribeiro M, de Paula Santos U, Bussacos MA, Terra-Filho M. Prevalence and risk of asthma symptoms among firefighters in São Paulo, Brazil: a population-based study. *Am J Ind Med.* 2009;52(3):261-269.

23. Kirkeleit J, Riise T, Bjørge T, Christiani DC. The healthy worker effect in cancer incidence studies. *American journal of epidemiology.* 2013;177(11):1218-1224.
24. Slottje P, Yzermans CJ, Korevaar JC, Hooiveld M, Vermeulen RCH. The population-based Occupational and Environmental Health Prospective Cohort Study (AMIGO) in The Netherlands. *BMJ Open.* 2014;4(11):e005858-e005858.
25. Moir W, Zeig-Owens R, Daniels RD, et al. Post-9/11 cancer incidence in World Trade Center-exposed New York City firefighters as compared to a pooled cohort of firefighters from San Francisco, Chicago and Philadelphia (9/11/2001-2009). *Am J Ind Med.* 2016;59(9):722-730.
26. Webber MP, Glaser MS, Weakley J, et al. Physician-diagnosed respiratory conditions and mental health symptoms 7-9 years following the World Trade Center disaster. *Am J Ind Med.* 2011;54(9):661-671.
27. Webber MP, Gustave J, Lee R, et al. Trends in respiratory symptoms of firefighters exposed to the world trade center disaster: 2001-2005. *Environmental health perspectives.* 2009;117(6):975-980.
28. Yip J, Webber MP, Zeig-Owens R, et al. FDNY and 9/11: Clinical services and health outcomes in World Trade Center-exposed firefighters and EMS workers from 2001 to 2016. *Am J Ind Med.* 2016;59(9):695-708.
29. Weakley J, Webber MP, Ye F, et al. Agreement between obstructive airways disease diagnoses from self-report questionnaires and medical records. *Preventive Medicine.* 2013;57(1):38-42.
30. Weakley J, Webber MP, Ye F, et al. Agreement between upper respiratory diagnoses from self-report questionnaires and medical records in an occupational health setting. *Am J Ind Med.* 2014;57(10):1181-1187.
31. Zeig-Owens R, Kablanian A, Webber MP, et al. Agreement Between Self-Reported and Confirmed Cancer Diagnoses in New York City Firefighters and EMS Workers, 2001-2011. *Public Health Rep.* 2016;131(1):153-159.
32. Sinclair M, O'Toole J, Malawaraarachchi M, Leder K. Comparison of response rates and cost-effectiveness for a community-based survey: postal, internet and telephone modes with generic or personalised recruitment approaches. *BMC Medical Research Methodology.* 2012;12(1):132.
33. Jepson C, Asch DA, Hershey JC, Ubel PA. In a mailed physician survey, questionnaire length had a threshold effect on response rate. *Journal of Clinical Epidemiology.* 2005;58(1):103-105.
34. Rothbaum J, Bee A. Coronavirus Infects Surveys, Too: Nonresponse Bias During the Pandemic in the CPS ASEC. 2020. https://www.census.gov/content/dam/Census/library/working-papers/2020/demo/sehsd-wp2020-10.pdf. Accessed December 21, 2020.
35. Blair E, Zinkhan GM. From the Editor: Nonresponse and Generalizability in Academic Research. *Journal of the Academy of Marketing Science.* 2006;34(1):4-7.

Table I. Original Data from National Institute for Occupational Safety and Health (NIOSH) for the Career Firefighter Health Study Cohort

Variable	Full CFHS Cohort (N=29,992) N (%)	CFHS Outreach Cohort Subpopulation (N=14,566) N (%)
SSN	27,945 (93.2)	14,544 (99.8)
Date of birth	29,979 (>99.9)	14,566 (100)
Race	29,085 (97.0)	14,456 (99.2)
Sex	29,891 (99.7)	14,566 (100)
Mailing address	22,888 (76.3)	14,492 (99.5)

Abbreviations: SSN = Social Security Number; CFHS = Career Firefighter Health Study

Table II. Demographic Comparison of Career Firefighter Health Study Outreach Cohort and WTC-Exposed FDNY Firefighters

Variable	Career Firefighter Health Study Outreach Cohort (N=14,566)	WTC-Exposed FDNY Firefighters (N=13,317)
Gender[1]		
Male	13,631 (93.6)	13,280 (99.7)
Female	935 (6.4)	37 (0.3)

Age[1,2]		
30-39	583 (4.0)	48 (0.4)
40-49	2,239 (15.4)	1,855 (13.9)
50-59	3,927 (27.0)	4,743 (35.6)
60-69	3,819 (26.2)	4,756 (35.7)
70-79	2,788 (19.1)	1,466 (11.0)
80+	1,210 (8.3)	449 (3.4)
Race/Ethnicity[1]		
Hispanic	1,203 (8.3)	500 (3.8)
White, Non-Hispanic	10,204 (70.0)	12,376 (92.9)
Black, Non-Hispanic	2,532 (17.4)	389 (2.9)
Other, Non-Hispanic	517 (3.5)	49 (0.4)
Unknown	110 (0.8)	3 (0.02)

[1]Chi square p<0.001 [2]Age as of 12/31/2020

Table III. Final Interviewing Status and Response Rates by Group from the Career Firefighter Health Study Outreach Cohort

Interview Status	San Francisco (N=2,697)	Philadelphia (N=4,182)	Chicago (N=7,687)	Total (N=14,566)
Completed Interviews (Phone)	122 (4.5)	149 (3.6)	172 (2.2)	443 (3.0)
Completed Interviews (Web)	940 (34.9)	1,148 (27.5)	1,907 (24.8)	3,995 (27.4)
Partial Completes[1]	101 (3.7)	145 (3.5)	278 (3.6)	524 (3.6)
Total Interviews	1,163 (43.1)	1,442 (34.5)	2,357 (30.7)	4,962 (34.1)
Final Non-Interviews				
Final Refusal by Respondent	42 (1.6)	43 (1.0)	76 (1.0)	161 (1.1)
Final Refusal by Other	267 (9.9)	204 (4.9)	576 (7.5)	1,047 (7.2)
Other Final Non-Interviews	1,148 (42.6)	1,925 (46.0)	3,421 (44.5)	6,494 (44.6)
Subject not Located	45 (1.7)	521 (12.5)	1,161 (15.1)	1,727 (11.9)
Total Final Non-Interviews	1,502 (55.7)	2,693 (64.4)	5,234 (68.1)	9,429 (64.7)
Ineligible Firefighters (Deceased)	32 (1.2)	47 (1.1)	96 (1.2)	175 (1.2)
Total Eligible Firefighters	2,665 (98.8)	4,135 (98.9)	7,591 (98.8)	14,391(98.8)

[1] Partial completes are firefighters that started the survey but did not complete the full survey.

Table IV. Demographic Comparison of Respondents and Non-Respondents from the Career Firefighter Health Study Outreach Cohort

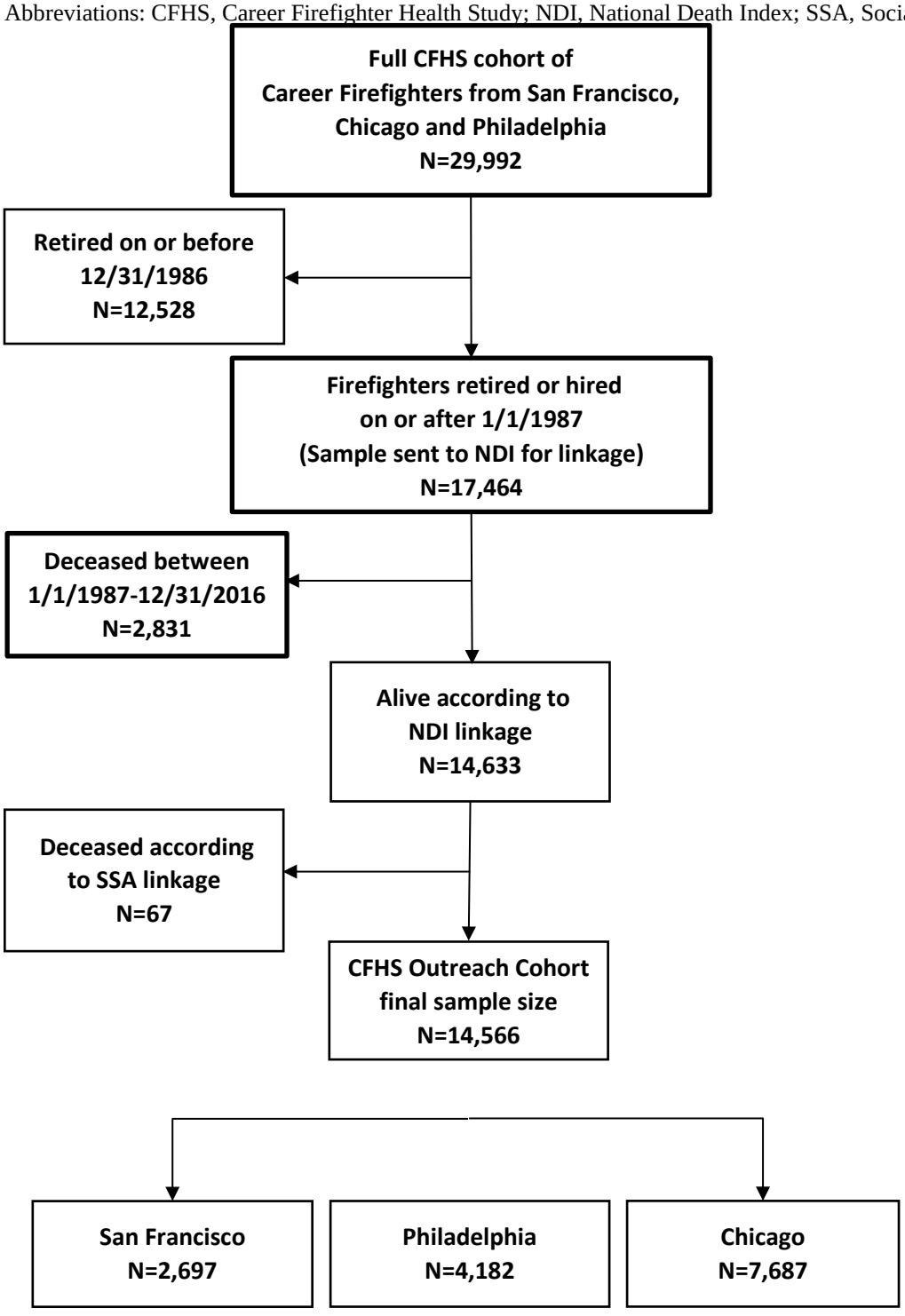
Variable	Non-Respondents (N=9,604)	Respondents (N=4,962)
Gender		
Male	8,972 (93.4)	4,659 (93.9)
Female	632 (6.6)	303 (6.1)
Age[1,2]		
30-39	453 (4.7)	130 (3.4)
40-49	1,619 (16.9)	620 (12.5)
50-59	2,646 (27.6)	1,281 (25.8)
60-69	2,366 (24.6)	1,453 (29.3)
70-79	1,678 (17.5)	1,110 (22.4)
80+	842 (8.8)	368 (7.4)
Race/Ethnicity[2]		
Hispanic	842 (8.8)	361 (7.3)
White, Non-Hispanic	6,358 (66.2)	3,846 (77.5)
Black, Non-Hispanic	2,016 (21.0)	516 (10.4)
Other, Non-Hispanic		

Unknown	309 (3.2) 79 (0.8)	208 (4.2) 31 (0.6)

[1]Age as of 12/31/2020

[2]Chi square p<0.001

Figure 1. Establishment of Career Firefighter Health Study Outreach Cohort
Figure 1 Legend:
Abbreviations: CFHS, Career Firefighter Health Study; NDI, National Death Index; SSA, Social Security Administration



Aim 3

Compare the post-9/11 prevalence and incidence of physical and mental health symptoms and diagnosed conditions in the FDNY FF Cohort and the Firefighter Comparison Cohort.

PTSD symptoms, depressive symptoms, and subjective cognitive concerns in WTC-exposed and non-WTC-exposed firefighters

Alexandra K. Mueller, MPH*; Ankura Singh, MPH*; Mayris P. Webber, DrPH; Charles B. Hall, PhD; David J. Prezant, MD; Rachel Zeig-Owens, DrPH

*contributed equally

Introduction

Occupational exposures related to firefighting have been shown to have negative impacts on both the physical and the mental health of firefighters.[1-4] Posttraumatic stress disorder (PTSD) and depression are among the most studied mental health conditions; in firefighters, they are often associated with potentially traumatic events (PTEs) from repeated occupational stressors like dangerous situations, unpredictable conditions, and witnessing injury and emotional distress,[5-9] and from acute traumatic experiences like a terrorist attack, manmade or natural disasters, or witnessing a death.[10-15] One systematic review found that the severity and duration of a disaster exposure are directly related to the development of PTSD and depression in cross-national samples, suggesting that exposure to severe acute traumatic events may outweigh protections gained from career experience and/or resiliency training.[16]

Until recently, cognitive function in firefighters was understudied, despite firefighters' exposure to common occupational stressors like smoke and sleep deprivation, which have been shown to have detrimental impacts on cognitive performance.[17,18] Other studies reported that thermal stress among those that work in hot environments may also lead to cognitive deficits.[19,20] Additionally, traumatic brain injury (TBI) may be related to an increased risk of reporting subjective memory impairment,[21] as well as to PTSD and depression.[22,23]

Studies of World Trade Center (WTC)-exposed rescue/recovery workers have found that those most exposed to the WTC disaster were at increased risk of developing PTSD symptoms and depressive symptoms.[15,24-27] In recent studies, we found that WTC exposure, PTSD symptoms, and depressive symptoms were associated with subjective cognitive concerns in Fire Department of the City of New York (FDNY) rescue/recovery workers,[12] with PTSD and depressive symptoms acting as mediators of the association between WTC exposure and cognitive concerns.[28] In a cohort of non-FDNY WTC responders, duration of WTC exposure and PTSD symptom severity were risk factors for reduced cognitive function.[29,30] Another study of WTC-exposed individuals found that the risk of experiencing confusion or memory loss, analogs for cognitive function, increased along with participants' number of other mental health conditions.[31]

While studies of WTC-exposed rescue/recovery workers have found associations between WTC exposure and the above mental health conditions, investigators have not previously had access to a comparison population consisting of non-WTC-exposed rescue/recovery workers. The current study was undertaken to compare levels of PTSD symptoms, depressive symptoms, and subjective cognitive concerns in WTC-exposed FDNY firefighters vs. in non-WTC-exposed firefighters from the Chicago, Philadelphia, and San Francisco fire departments who completed a health questionnaire for the Career Firefighter Health Study (CFHS).[32] We also sought to identify demographic, lifestyle, and other characteristics associated with each of these mental health conditions in the firefighter cohorts.

Methods

Study Population

Male WTC-exposed FDNY and non-WTC-exposed Chicago Fire Department (CFD), Philadelphia Fire Department (PFD), and San Francisco Fire Department (SFFD) firefighters who were actively employed by their fire department on 9/11/2001, completed a self-administered health questionnaire with mental health screening measures, and provided written informed consent were included in this study. FDNY firefighters who performed rescue/recovery work at the WTC site any time between 9/11/2001 and 7/25/2002 were considered WTC-exposed. Of the 10,003 male firefighters in the FDNY source population, 1,537 firefighters were excluded because their last routine health monitoring examination

at FDNY was before 3/1/2018, the date the subjective cognitive assessment was added to FDNY's self-administered health monitoring questionnaire. The final FDNY population included 8,466 firefighters.

The original CFHS source population consisted of 29,992 professional firefighters from CFD, PFD, and SFFD whose information was originally obtained by the National Institute for Occupational Safety and Health (NIOSH) from the fire department rosters.[33] There were 8,813 male CFHS members who were actively employed on 9/11/2001; by 12/31/2020, 2,866 had completed the CFHS self-administered health survey, a questionnaire similar to FDNY's health questionnaire.[32] Of these individuals, 251 respondents reported some type of participation in the WTC rescue/recovery effort between 9/11/2001 and 7/25/2002, and were excluded from the current study. The final non-WTC-exposed firefighter population for analyses included 2,615 firefighters.

This study was approved by the Albert Einstein College of Medicine Institutional Review Board.

Demographic and Lifestyle Information

FDNY participants' dates of birth and race/ethnicity were available via the FDNY employee database, and WTC exposure level, defined by arrival time at the WTC site, was self-reported on the first post-9/11 health monitoring questionnaire.[34] Non-WTC-exposed firefighters provided their race/ethnicity information via the CFHS health questionnaire; their dates of birth and employment were available from the fire department roster data. Through the FDNY and CFHS health questionnaires, all participants also reported education level, smoking status (current, former, or never smoker), current alcohol use/binge drinking frequency, and whether they sought treatment for a mental health condition in the past year. FDNY participants' most recent questionnaire data were used.

Health-Related Quality of Life

The FDNY and CFHS questionnaires also contained the 12-item Short-Form Health Survey (SF-12), which measured participants' health-related quality of life.[35] Each participant received two composite scores when completing the SF-12: the Physical Component Summary (PCS) and Mental Component Summary (MCS) scales, as detailed in previous studies.[36,37] Scores of 50 on the SF-12 PCS and MCS represent the average self-rated physical and mental health-related quality of life, respectively, in the US general population. Lower scores correspond to worse health-related quality of life.

PTSD, Depression, and Subjective Cognition Assessment

Previously validated mental health screening instruments were included in both the FDNY and CFHS health questionnaires. We used the 17-item PTSD Checklist Specific (PCL-S) to measure PTSD symptoms.[38-40] The Life Events Checklist, which assessed participants' most traumatic experiences, was included in the health questionnaires along with the PCL-S.[41] In the FDNY questionnaire, WTC exposure was added to the list of options. Both FDNY and CFHS participants identified their index trauma prior to completing the PCL-S by indicating which experience from the Life Events Checklist was most traumatic to them. The 20-item Center for Epidemiologic Studies Depression Scale (CES-D)[42] and 14-item Cognitive Function Instrument (CFI)[43-45] assessed depressive symptoms and subjective cognitive concerns, respectively, as described in our previous studies.[12,28] CFI items measured whether participants felt that they had experienced cognitive and/or functional decline over the past year. Participants were asked if certain cognitive and functional abilities had declined compared to one year ago and received one point for every "yes" answer, half a point for every "maybe", and zero points for every "no". For each mental health screening instrument, higher scores corresponded to greater symptoms. A positive screen for probable PTSD was defined as having PCL-S score $\geq$44;[39] for probable depression, it was CES-D score $\geq$16;[42] and for subjective cognitive change, we used a cutoff of CFI score $\geq$2.[12] Hereafter, we refer to these outcomes as PTSD, depression, and subjective cognitive change, respectively.

Statistical Analyses

We used proportions (%), means (±SD), and medians (IQR), as appropriate, to describe demographic and other characteristics of the FDNY, CFD, PFD, and SFFD groups. Multivariable linear regression models stratified by fire department examined which variables, if any, were similarly associated with PCL-S, CES-D, and CFI scores in each department. The covariates were selected based on their previously established associations with PTSD, depression, and/or cognitive function.[46-49] The models included age at questionnaire completion, race/ethnicity, education level, smoking status, current excess alcohol use, and other mental health symptom scores as covariates; CES-D score was not included as a covariate in models predicting PCL-S score, and vice versa, due to the collinearity of these two variables (Pearson correlation $r=0.83$; $p<0.001$). Covariate data were centered at the mean values for the study population (59 years

of age; PCL-S score of 25; CES-D score of 8; CFI score of 2) or the reference values (white race; high school or some college education; never smoker; moderate alcohol use without binge drinking).

We then estimated associations between WTC exposure, assessed as a binary variable (yes/no), and mental health symptom scores using multivariable linear regression analyses: first controlling only for demographic characteristics and subsequently controlling for all potential confounders stated above. In a sensitivity analysis, we ran multivariable logistic regression models using a positive mental health screening result, as defined by the above cutoff scores, as the outcome. We again fit two models estimating the associations with WTC exposure, one controlling for demographics only, and the second controlling for all of the previously identified covariates.

Data analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). We reported two-sided p-values, considered statistically significant when $p<0.05$.

Results

Characteristics of the 8,466 FDNY, 1,195 CFD, 770 PFD, and 650 SFFD male firefighters in the final study population are displayed in Table I. Members of the source population who were excluded from the study were similar in age to the study population, but were more likely to be retired/deceased (data not shown). Among those included, WTC-exposed FDNY firefighters were younger, on average, and more likely to be white than those in the non-WTC-exposed firefighter cohorts. The FDNY group also had greater proportions of individuals with a bachelor's (or higher) degree and never smokers than the CFD and PFD groups; FDNY and SFFD participants were similar in education level and smoking status. The average physical health-related quality of life scores were lower (worse) for WTC-exposed firefighters than for non-WTC-exposed firefighters, while the average mental health-related quality of life scores were similar.

Table I also shows the crude mental health symptom scores in each of the firefighter cohorts. Average PCL-S and CES-D scores were similar in FDNY, CFD, and SFFD participants, but higher (worse) in those from PFD. The non-WTC-exposed firefighter cohorts all had the higher (worse) median CFI scores than the FDNY group.

PTSD Symptoms in Each Firefighter Cohort

All participants selected traumatic life events they had experienced, if any, on the Life Events Checklist prior to completing the PCL-S. Among WTC-exposed firefighters who reported experiencing at least one traumatic event, 79.0% indicated that WTC exposure was their most traumatic experience, or index trauma. The second most common index trauma among WTC-exposed firefighters was the non-WTC-related unexpected death of a relative, close friend, or coworker (10.2%). This was also the most common index trauma among non-WTC-exposed firefighters (43.1%), followed by 25.6% reporting a severe accident, injury, or illness.

Table II shows variables associated with PTSD symptoms when using multivariable linear regression analyses stratified by department. In each of the cohorts, after adjusting for other covariates, higher CFI scores corresponded to higher PCL-S scores, and older age was associated with lower PCL-S scores. Also shown in Table II are the model intercepts, or adjusted mean PCL-S scores, for an average member of the study population by fire department. Frequent binge drinking and abstaining from alcohol use were both associated with a higher PCL-S score in FDNY, compared with moderate alcohol use/no binge drinking. The same associations were not seen in the other firefighter cohorts (CFD, PFD, SFFD).

Depressive Symptoms in Each Firefighter Cohort

In stratified analyses in which depressive symptoms were the outcome (Table III), as with PTSD, we observed that increased CFI scores were consistently associated with greater CES-D scores, while older age was linked to lower CES-D scores. Smoking was associated with higher CES-D scores in FDNY and CFD firefighters, but not in the other firefighter cohorts. We also observed that in FDNY, but not the other firefighter cohorts, frequent binge drinking and abstaining from alcohol use were both associated with higher CES-D scores, compared with moderate alcohol use/no binge drinking.

Subjective Cognitive Concerns in Each Firefighter Cohort

When assessing factors associated with subjective cognitive concerns, we found associations between older age and greater CFI scores in the firefighter cohorts (Table IV), in addition to observing the same associations of PCL-S and CES-D scores with CFI scores stated above. The WTC-exposed FDNY cohort had a lower adjusted mean CFI score, when controlling for covariates, than the other firefighter cohorts. Binge drinking was also associated with modestly elevated CFI scores in FDNY, CFD and PFD cohorts, but not SFFD.

WTC Exposure and Mental Health Symptoms

Because adjusted mean PCL-S and CES-D scores and their associated variables varied in the three non-WTC-exposed firefighter cohorts, we determined it was inappropriate to combine the three cohorts as a reference category to estimate associations between WTC exposure and PCL-S score or WTC exposure and CES-D score. We were able to do so when assessing the association between WTC exposure and CFI score. We observed that WTC-exposed firefighters had a significantly lower CFI score (β=-0.76±0.06, $p<0.001$) than non-WTC-exposed firefighters in a multivariable linear regression model controlling for for age, race, and education level (Table V). An analysis that controlled for smoking status, excess alcohol use, and CES-D score in addition to the demographic variables showed similar results (β=-0.69±0.05, $p<0.001$).

Sensitivity analyses examined associations between WTC exposure and subjective cognitive change (CFI score ≥2) in multivariable logistic regression models. WTC-exposed firefighters had significantly lower odds of subjective cognitive change when controlling only for demographics (OR=0.49, 95% CI=0.45-0.54), as well as when controlling for demographics, smoking status, excess alcohol use, and positive depression screening (OR=0.44, 95% CI=0.40-0.50).

Discussion

This study is unique as it is the first to look at mental health outcomes in WTC-exposed firefighters compared with these outcomes in a similar, non-WTC-exposed, firefighter occupational cohort. Specifically, we examined PTSD symptoms, depressive symptoms, and subjective cognitive concerns in WTC-exposed FDNY firefighters compared with non-WTC-exposed firefighters. In the study population of over 10,000 firefighters, WTC exposure was associated with *fewer* cognitive concerns after controlling for demographics, smoking, excess alcohol use, and PTSD symptom scores. WTC-exposed firefighters had a 56% *lower* odds of subjective cognitive change in the last year, defined as a score ≥2 on the CFI compared with non-WTC-exposed firefighters.

In multivariable-adjusted analyses that assessed each firefighter subpopulation separately, we found that an average member of the WTC-exposed FDNY firefighter cohort had adjusted mean PTSD and depressive symptom scores of 25.8±0.2 and 9.1±0.2, respectively. In the non-WTC-exposed firefighter subpopulations, adjusted mean PTSD symptom scores ranged from 23.5±0.6 to 25.7±0.8, and adjusted mean depressive symptom scores ranged from 7.3±0.5 to 9.4±0.6. When evaluating PTSD symptoms and depressive symptoms in the WTC-exposed and non-WTC-exposed cohorts, we determined it was inappropriate to perform analyses in which the three non-WTC-exposed firefighter cohorts were combined, due to their varied levels of PTSD and depressive symptoms. To date, the literature about risk factors for PTSD in firefighters is mixed. Much of the research suggests that repeated exposure to stress increases the risk of developing stress-related diseases.[50-52] However, there is also evidence to support the idea that professional or career firefighters have greater resilience to stress-related diseases due to better training and experience compared to volunteers.[51,52] Our data show that PTSD and depressive symptom scores in each cohort were, on average, well below published screening thresholds for probable PTSD and depression.[39,42] As all cohorts were comprised entirely of professional firefighters, we expect that training experiences were similar across cohorts. Instead, the severity of the WTC trauma may have played a larger role. Amir et al. examined the association between severity of trauma exposure (battlefield experience, civilian terrorism, and work or traffic accidents) and PTSD symptoms and found that the more severe the trauma exposure, the more severe the PTSD symptoms.[53] A 2019 study by Pozza et al. found that victims of terrorist attacks had significantly greater general PTSD severity compared with those who had experienced other PTEs.[54] In prior screening studies, we and others have found that greater WTC exposure is associated with an increased risk of PTSD and depression.[12,15,24,25,27] Of the WTC-exposed group, 79% reported that the WTC disaster was their most traumatic experience. Among non-WTC-exposed firefighters, the most traumatic experience was the unexpected death of a relative, close friend, or coworker (43%).

We found PTSD and depressive symptom scores to be highly correlated. Comorbidity of mental health outcomes is not uncommon. O'Donnell et al. found that psychopathology following trauma exposure was better explained through a generalized traumatic stress factor that included both PTSD and depression as opposed to each individually.[55] Both conditions are also often associated with other mental health concerns, like alcohol use disorders;[15,56-58] accordingly, we controlled for alcohol use in the analyses. PTSD and depression have also been linked to reduced cognitive functioning in WTC-exposed individuals, as well as in other populations.[46,47,49,59]

We previously observed associations of PTSD and depressive symptoms with subjective cognitive change, and found that PTSD and depressive symptoms mediate the association between WTC exposure and subjective cognitive concerns. In the current analysis, we found *fewer* subjective cognitive concerns among WTC-exposed firefighters

compared with the non-exposed firefighters. While this difference was statistically significant, the WTC-exposed group reported, on average, only one less cognitive symptom out of a 14-item instrument. It is also important to note that in our prior studies, we used internal comparisons by WTC exposure intensity, and observed an exposure-response gradient where cognitive complaints increased in those most highly exposed. Clouston et al. compared non-FDNY WTC-exposed responders' performance on an objective cognitive battery with age-matched published normative data from clinical trials, and found that WTC responders' cognitive function was worse than expected.[29] The current study used an external comparison group that is occupationally similar, which is important given the ubiquity of firefighting-related health concerns.[1-4] It is possible the differences in perceived cognitive decline between the WTC-exposed and non-exposed groups may include uncontrolled residual confounding (such as traumatic brain injuries) or cultural differences. Future studies investigating cognition in these cohorts will need an objective cognitive assessment to confirm any differences in cognitive function between the two groups.

We found that older age was associated with worse self-assessed cognitive function, but better PTSD and depression outcomes. This is supported through the literature, as it is widely accepted that cognitive function tends to decline over time, often referred to as age-related cognitive decline.[60-62] More interestingly, PTSD symptom severity has also been reported to improve over time. Yehuda et al. conducted a ten-year longitudinal study of PTSD in Holocaust survivors and found that symptom severity declined between the two time points.[63] Posttraumatic growth is the positive psychological change that can occur after a traumatic event.[64] While there is limited research examining long-term trajectory of posttraumatic growth, a 2020 study of WTC-exposed individuals found that it was present 15 years after the WTC disaster.[64] Bluvstein et al. found that posttraumatic stress symptoms were positively associated with posttraumatic growth.[65] This suggests that posttraumatic growth can follow posttraumatic stress and improve over time, a finding supported by our work. Prior work has shown that increased social support among the elderly is associated with improved cognitive function.[66-69] Further, Stanley et al. found that greater perceived organizational support attenuated PTSD symptom severity in US firefighters.[70] These findings support continued access to mental health services, which may improve PTSD symptoms and cognitive function over time.

We note that WTC-exposed FDNY firefighters may have greater access to mental health treatment, via the WTC Health Program, than the other three firefighter cohorts. It is possible that treatment for PTSD and/or depression reduced cognitive concerns,[71,72] as well as PTSD and depressive symptoms, within the FDNY cohort; however, we observed that FDNY and the three non-WTC-exposed firefighter cohorts had similar proportions of mental health treatment-seeking patients (10.6%, 6.4%, 10.1% and 6.3% in FDNY, CFD, PFD and SFFD, respectively).

Another limitation of this study was our use of screening instruments as opposed to diagnoses; the results are therefore only generalizable for symptoms of PTSD, depression, and cognitive decline, not diagnoses. However, these screening instruments measure the same outcome for each cohort and do not depend on availability of mental health services for diagnosis. The PCL and CES-D have been validated in WTC-exposed firefighters, as well as in other populations.[38,40,42,73,74] The CFI was validated in older adults who were determined to be free of clinical dementia or impairment at baseline;[43,45] in these populations, higher baseline CFI scores predicted dementia and worse performance on an objective cognitive measure.[43,75,76] Future studies are planned that will assess cognitive function among firefighters using an objective cognitive assessment, as the CFI is not yet validated in this cohort.

Further limitations of this study include the potential for selection bias, as 85% of the WTC-exposed FDNY source population and 30% of the CFHS source population were included in the final sample, the exclusion of women due to low numbers in the cohorts, and uncontrolled confounding, particularly surrounding cultural differences in self-reporting potentially stigmatic symptoms. Use of an objective cognitive measure could be useful in addressing the latter concern. However, the surveys were self-administered for all participants, the response method was similar for all firefighters, and our analyses controlled for demographic variables that could potentially affect response variation. Finally, we observed that PTSD and depressive symptom scores were highly correlated in our study population, and were therefore not included in the multivariable models simultaneously.

In conclusion, twenty years after the attacks on September 11, 2001, 8% of WTC-exposed firefighters had probable PTSD and 17% had probable depression. While we estimated adjusted mean PTSD and depressive symptom scores in the WTC-exposed and non-WTC-exposed firefighter cohorts, we were unable to test for associations between WTC exposure and PTSD symptoms or depressive symptoms due to differences between the non-WTC-exposed cohorts. We did find, however, that WTC-exposed firefighters had fewer cognitive concerns compared with non-WTC-exposed firefighters. Longitudinal follow-up is needed to further assess PTSD, depression, and cognitive symptom trajectories in firefighter populations as they age. Comparing cohorts in this manner allows for a better understanding of the lasting effect of the

exposure to the WTC disaster and adds to the growing body of research surrounding occupational hazards and mental health.

References

1. Crawford JO, Graveling RA. Non-cancer occupational health risks in firefighters. *Occup Med (Lond).* 2012;62(7):485-495.
2. McDonough SL, Phillips JS, Twilbeck TJ. Determining Best Practices to Reduce Occupational Health Risks in Firefighters. *J Strength Cond Res.* 2015;29(7):2041-2044.
3. Melius J. Occupational health for firefighters. *Occup Med.* 2001;16(1):101-108.
4. Sawhney G, Jennings KS, Britt TW, Sliter MT. Occupational stress and mental health symptoms: Examining the moderating effect of work recovery strategies in firefighters. *J Occup Health Psychol.* 2018;23(3):443-456.
5. Harvey SB, Milligan-Saville JS, Paterson HM, et al. The mental health of fire-fighters: An examination of the impact of repeated trauma exposure. *Aust N Z J Psychiatry.* 2016;50(7):649-658.
6. Jahnke SA, Poston WS, Haddock CK, Murphy B. Firefighting and mental health: Experiences of repeated exposure to trauma. *Work.* 2016;53(4):737-744.
7. Lee JH, Lee D, Kim J, Jeon K, Sim M. Duty-Related Trauma Exposure and Posttraumatic Stress Symptoms in Professional Firefighters. *J Trauma Stress.* 2017;30(2):133-141.
8. Milligan-Saville J, Choi I, Deady M, et al. The impact of trauma exposure on the development of PTSD and psychological distress in a volunteer fire service. *Psychiatry Res.* 2018;270:1110-1115.
9. Skogstad M, Skorstad M, Lie A, Conradi HS, Heir T, Weisaeth L. Work-related post-traumatic stress disorder. *Occup Med (Lond).* 2013;63(3):175-182.
10. Katsavouni F, Bebetsos E, Malliou P, Beneka A. The relationship between burnout, PTSD symptoms and injuries in firefighters. *Occup Med (Lond).* 2016;66(1):32-37.
11. Psarros C, Theleritis C, Kokras N, et al. Personality characteristics and individual factors associated with PTSD in firefighters one month after extended wildfires. *Nord J Psychiatry.* 2018;72(1):17-23.
12. Singh A, Zeig-Owens R, Hall CB, et al. World Trade Center exposure, post-traumatic stress disorder, and subjective cognitive concerns in a cohort of rescue/recovery workers. *Acta psychiatrica Scandinavica.* 2020;141(3):275-284.
13. Skogstad L, Heir T, Hauff E, Ekeberg O. Post-traumatic stress among rescue workers after terror attacks in Norway. *Occup Med (Lond).* 2016;66(7):528-535.
14. Van Eerd D, Irvin E, Harbin S, Mahood Q, Tiong M. Occupational exposure and post-traumatic stress disorder: A rapid review. *Work.* 2021;68(3):721-731.
15. Berninger A, Webber MP, Cohen HW, et al. Trends of elevated PTSD risk in firefighters exposed to the World Trade Center disaster: 2001-2005. *Public health reports (Washington, DC : 1974).* 2010;125(4):556-566.
16. Wagner SL, White N, Randall C, et al. Mental Disorders in Firefighters Following Large-Scale Disaster. *Disaster Med Public Health Prep.* 2020:1-14.
17. Hemmatjo R, Motamedzade M, Aliabadi M, Kalatpour O, Farhadian M. The effect of artificial smoke compound on physiological responses, cognitive functions and work performance during firefighting activities in a smoke-diving room: an intervention study. *Int J Occup Saf Ergon.* 2018;24(3):358-365.
18. Kujawski S, Slomko J, Tafil-Klawe M, et al. The impact of total sleep deprivation upon cognitive functioning in firefighters. *Neuropsychiatr Dis Treat.* 2018;14:1171-1181.
19. Mazloumi A, Golbabaei F, Mahmood Khani S, et al. Evaluating Effects of Heat Stress on Cognitive Function among Workers in a Hot Industry. *Health Promot Perspect.* 2014;4(2):240-246.
20. Piil JF, Lundbye-Jensen J, Christiansen L, et al. High prevalence of hypohydration in occupations with heat stress-Perspectives for performance in combined cognitive and motor tasks. *PLoS One.* 2018;13(10):e0205321.
21. Gardner RC, Langa KM, Yaffe K. Subjective and objective cognitive function among older adults with a history of traumatic brain injury: A population-based cohort study. *PLoS Med.* 2017;14(3):e1002246.
22. Strack JE, Torres VA, Pennington ML, et al. Psychological distress and line-of-duty head injuries in firefighters. *Occup Med (Lond).* 2021;71(2):99-104.

23. Torres VA, Strack JE, Dolan S, et al. Identifying Frequency of Mild Traumatic Brain Injury in Firefighters. *Workplace Health Saf.* 2020;68(10):468-475.
24. Jordan HT, Osahan S, Li J, et al. Persistent mental and physical health impact of exposure to the September 11, 2001 World Trade Center terrorist attacks. *Environmental health : a global access science source.* 2019;18(1):12.
25. Soo J, Webber MP, Gustave J, et al. Trends in probable PTSD in firefighters exposed to the World Trade Center disaster, 2001-2010. *Disaster Med Public Health Prep.* 2011;5 Suppl 2:S197-203.
26. Yip J, Webber MP, Zeig-Owens R, et al. FDNY and 9/11: Clinical services and health outcomes in World Trade Center-exposed firefighters and EMS workers from 2001 to 2016. *American journal of industrial medicine.* 2016;59(9):695-708.
27. Yip J, Zeig-Owens R, Webber MP, et al. World Trade Center-related physical and mental health burden among New York City Fire Department emergency medical service workers. *Occupational and environmental medicine.* 2016;73(1):13-20.
28. Singh A, Zeig-Owens R, Rabin L, et al. PTSD and Depressive Symptoms as Potential Mediators of the Association between World Trade Center Exposure and Subjective Cognitive Concerns in Rescue/Recovery Workers. *International journal of environmental research and public health.* 2020;17(16).
29. Clouston S, Pietrzak RH, Kotov R, et al. Traumatic exposures, posttraumatic stress disorder, and cognitive functioning in World Trade Center responders. *Alzheimer's & dementia (New York, N Y).* 2017;3(4):593-602.
30. Clouston SAP, Diminich ED, Kotov R, et al. Incidence of mild cognitive impairment in World Trade Center responders: Long-term consequences of re-experiencing the events on 9/11/2001. *Alzheimer's & dementia (Amsterdam, Netherlands).* 2019;11:628-636.
31. Alper HE, Tuly RA, Seil K, Brite J. Post-9/11 Mental Health Comorbidity Predicts Self-Reported Confusion or Memory Loss in World Trade Center Health Registry Enrollees. *International journal of environmental research and public health.* 2020;17(19).
32. Brackbill RM, Kahn AR, Li J, et al. Combining Three Cohorts of World Trade Center Rescue/Recovery Workers for Assessing Cancer Incidence and Mortality. *Int J Environ Res Public Health.* 2021;18(4).
33. Daniels RD, Kubale TL, Yiin JH, et al. Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950-2009). *Occupational and environmental medicine.* 2014;71(6):388-397.
34. Aldrich TK, Vossbrinck M, Zeig-Owens R, et al. Lung Function Trajectories in World Trade Center-Exposed New York City Firefighters Over 13 Years: The Roles of Smoking and Smoking Cessation. *Chest.* 2016;149(6):1419-1427.
35. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical care.* 1996;34(3):220-233.
36. Ware J, Ma K, Tuner-bowker D, Gandek B. Version 2 of the SF12 health survey. 2002.
37. Yip J, Zeig-Owens R, Hall CB, et al. Health Conditions as Mediators of the Association Between World Trade Center Exposure and Health-Related Quality of Life in Firefighters and EMS Workers. *Journal of occupational and environmental medicine.* 2016;58(2):200-206.
38. Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the PTSD Checklist (PCL). *Behaviour research and therapy.* 1996;34(8):669-673.
39. Ruggiero KJ, Del Ben K, Scotti JR, Rabalais AE. Psychometric properties of the PTSD Checklist-Civilian Version. *J Trauma Stress.* 2003;16(5):495-502.
40. Wilkins KC, Lang AJ, Norman SB. Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian, and specific versions. *Depression and Anxiety.* 2011;28(7):596-606.
41. Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric Properties of the Life Events Checklist. *Assessment.* 2004;11(4):330-341.
42. Radloff LS. The CES-D Scale:A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement.* 1977;1(3):385-401.
43. Amariglio RE, Donohue MC, Marshall GA, et al. Tracking early decline in cognitive function in older individuals at risk for Alzheimer disease dementia: the Alzheimer's Disease Cooperative Study Cognitive Function Instrument. *JAMA neurology.* 2015;72(4):446-454.
44. Ferris SH, Aisen PS, Cummings J, et al. ADCS Prevention Instrument Project: overview and initial results. *Alzheimer disease and associated disorders.* 2006;20(4 Suppl 3):S109-123.

45. Walsh SP, Raman R, Jones KB, Aisen PS. ADCS Prevention Instrument Project: the Mail-In Cognitive Function Screening Instrument (MCFSI). *Alzheimer disease and associated disorders.* 2006;20(4 Suppl 3):S170-178.
46. Baumgart M, Snyder HM, Carrillo MC, Fazio S, Kim H, Johns H. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimer's & dementia : the journal of the Alzheimer's Association.* 2015;11(6):718-726.
47. Lopez OL, Jagust WJ, Dulberg C, et al. Risk Factors for Mild Cognitive Impairment in the Cardiovascular Health Study Cognition Study: Part 2. *Archives of Neurology.* 2003;60(10):1394-1399.
48. Tervo S, Kivipelto M, Hanninen T, et al. Incidence and risk factors for mild cognitive impairment: a population-based three-year follow-up study of cognitively healthy elderly subjects. *Dementia and geriatric cognitive disorders.* 2004;17(3):196-203.
49. Sumner JA, Hagan K, Grodstein F, Roberts AL, Harel B, Koenen KC. Posttraumatic stress disorder symptoms and cognitive function in a large cohort of middle-aged women. *Depress Anxiety.* 2017;34(4):356-366.
50. Fraess-Phillips AW, S.; Harris, R.L. Firefighters and traumatic stress: a review. *International Journal of Emergency Services.* 2017;6(1):67-80.
51. Gulliver SB, Zimering RT, Knight J, et al. A prospective study of firefighters' PTSD and depression symptoms: The first 3 years of service. *Psychol Trauma.* 2021;13(1):44-55.
52. Kim JI, Park H, Kim JH. The mediation effect of PTSD, perceived job stress and resilience on the relationship between trauma exposure and the development of depression and alcohol use problems in Korean firefighters: A cross-sectional study. *J Affect Disord.* 2018;229:450-455.
53. Amir M, Kaplan Z, Kotler M. Type of trauma, severity of posttraumatic stress disorder core symptoms, and associated features. *J Gen Psychol.* 1996;123(4):341-351.
54. Pozza A, Bossini L, Ferretti F, et al. The Effects of Terrorist Attacks on Symptom Clusters of PTSD: a Comparison with Victims of Other Traumatic Events. *Psychiatr Q.* 2019;90(3):587-599.
55. O'Donnell ML, Creamer M, Pattison P. Posttraumatic stress disorder and depression following trauma: understanding comorbidity. *Am J Psychiatry.* 2004;161(8):1390-1396.
56. Bartlett BA, Smith LJ, Lebeaut A, Tran JK, Vujanovic AA. PTSD symptom severity and impulsivity among firefighters: Associations with alcohol use. *Psychiatry Res.* 2019;278:315-323.
57. Gallyer AJ, Dougherty SP, Gai AR, et al. Problematic alcohol use and suicidal ideation among firefighters: A multi-study investigation of the explanatory roles of perceived burdensomeness and thwarted belongingness. *J Affect Disord.* 2018;238:281-288.
58. Paulus DJ, Vujanovic AA, Schuhmann BB, Smith LJ, Tran J. Main and interactive effects of depression and posttraumatic stress in relation to alcohol dependence among urban male firefighters. *Psychiatry Res.* 2017;251:69-75.
59. Bhattarai JJ, Oehlert ME, Multon KD, Sumerall SW. Dementia and Cognitive Impairment Among U.S. Veterans With a History of MDD or PTSD: A Retrospective Cohort Study Based on Sex and Race. *Journal of aging and health.* 2019;31(8):1398-1422.
60. Harada CN, Natelson Love MC, Triebel KL. Normal cognitive aging. *Clin Geriatr Med.* 2013;29(4):737-752.
61. Langa KM, Levine DA. The diagnosis and management of mild cognitive impairment: a clinical review. *JAMA.* 2014;312(23):2551-2561.
62. Soldan A, Pettigrew C, Cai Q, et al. Cognitive reserve and long-term change in cognition in aging and preclinical Alzheimer's disease. *Neurobiol Aging.* 2017;60:164-172.
63. Yehuda R, Schmeidler J, Labinsky E, et al. Ten-year follow-up study of PTSD diagnosis, symptom severity and psychosocial indices in aging holocaust survivors. *Acta psychiatrica Scandinavica.* 2009;119(1):25-34.
64. Pollari CD, Brite J, Brackbill RM, et al. World Trade Center Exposure and Posttraumatic Growth: Assessing Positive Psychological Change 15 Years after 9/11. *International journal of environmental research and public health.* 2020;18(1).
65. Bluvstein I, Moravchick L, Sheps D, Schreiber S, Bloch M. Posttraumatic growth, posttraumatic stress symptoms and mental health among coronary heart disease survivors. *J Clin Psychol Med Settings.* 2013;20(2):164-172.
66. Ayotte BJ, Allaire JC, Whitfield KE. Social support, physical functioning, and cognitive functioning among older African American adults. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn.* 2013;20(4):494-510.
67. Costa-Cordella S, Arevalo-Romero C, Parada FJ, Rossi A. Social Support and Cognition: A Systematic Review. *Front Psychol.* 2021;12:637060.

68. Oremus M, Konnert C, Law J, Maxwell CJ, O'Connell ME, Tyas SL. Social support and cognitive function in middle- and older-aged adults: descriptive analysis of CLSA tracking data. *Eur J Public Health.* 2019;29(6):1084-1089.
69. Zuelsdorff ML, Koscik RL, Okonkwo OC, et al. Social support and verbal interaction are differentially associated with cognitive function in midlife and older age. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn.* 2019;26(2):144-160.
70. Stanley IH, Hom MA, Chu C, et al. Perceptions of belongingness and social support attenuate PTSD symptom severity among firefighters: A multistudy investigation. *Psychol Serv.* 2019;16(4):543-555.
71. Fedoroff IC, Taylor S, Asmundson GJG, Koch WJ. Cognitive factors in traumatic stress reactions: Predicting PTSD symptoms from anxiety sensitivity and beliefs about harmful events. *Behavioural and Cognitive Psychotherapy.* 2000;28(1):5-15.
72. Rosenblat JD, Kakar R, McIntyre RS. The Cognitive Effects of Antidepressants in Major Depressive Disorder: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Int J Neuropsychopharmacol.* 2015;19(2).
73. Chiu S, Webber MP, Zeig-Owens R, et al. Validation of the Center for Epidemiologic Studies Depression Scale in screening for major depressive disorder among retired firefighters exposed to the World Trade Center disaster. *J Affect Disord.* 2010;121(3):212-219.
74. Chiu S, Webber MP, Zeig-Owens R, et al. Performance characteristics of the PTSD Checklist in retired firefighters exposed to the World Trade Center disaster. *Ann Clin Psychiatry.* 2011;23(2):95-104.
75. Li C, Neugroschl J, Luo X, et al. The Utility of the Cognitive Function Instrument (CFI) to Detect Cognitive Decline in Non-Demented Older Adults. *Journal of Alzheimer's disease : JAD.* 2017;60(2):427-437.
76. Chipi E, Montanucci C, Eusebi P, et al. The Italian version of Cognitive Function Instrument (CFI) for tracking changes in healthy elderly: results at 1-year follow-up. *Neurological Sciences.* 2019;40(10):2147-2153.

Table 1

	WTC-exposed	Non-WTC-exposed		
	FDNY	CFD	PFD	SFFD
n	8466	1195	770	650
Age at exam (SD)	58.34 (7.44)	61.28 (8.41)	63.81 (8.93)	62.01 (8.82)
Race (%)				
Non-Hispanic White	8002 (94.52)	894 (74.81)	606 (78.70)	397 (61.08)
Non-Hispanic Black	182 (2.15)	107 (8.95)	111 (14.42)	44 (6.77)
Hispanic	257 (3.04)	140 (11.72)	24 (3.12)	84 (12.92)
Other race[a]	25 (0.3)	54 (4.52)	29 (3.77)	125 (19.23)
Education (%)				
High school or some college	4638 (54.78)	710 (59.41)	553 (71.82)	280 (43.08)
Associates or RN	1108 (13.09)	181 (15.15)	96 (12.47)	132 (20.31)
Bachelor's degree or higher	2720 (32.13)	304 (25.44)	121 (15.71)	238 (36.62)
Smoking status (%)				
Never	5707 (67.42)	702 (58.74)	349 (45.32)	427 (65.69)
Former	2560 (30.24)	408 (34.14)	354 (45.97)	203 (31.23)
Current	198 (2.34)	85 (7.11)	67 (8.70)	20 (3.08)
HR QoL (SF-12) (SD)				
PCS score	46.51 (10.19)	49.72 (8.58)	48.09 (9.51)	49.38 (9.37)
MCS score	52.80 (9.50)	52.94 (8.64)	51.37 (9.64)	52.31 (8.58)
PCL-S score (SD)	24.98 (10.82)	24.50 (9.38)	27.05 (11.19)	24.68 (9.00)
CES-D score (SD)	8.45 (9.07)	8.48 (8.04)	9.91 (8.99)	8.87 (8.07)
Median CFI score (IQR)	0 (0–2)	1 (0–3.5)	2 (0.5–4.5)	1 (0–3)
Probable PTSD (%)	671 (7.92)	64 (5.36)	68 (8.83)	28 (4.31)
Probable depression (%)	1408 (16.63)	182 (15.23)	168 (21.82)	110 (16.92)
Cognitive concerns ≥2 (%)	2296 (27.12)	517 (43.26)	417 (54.16)	271 (41.69)
Sought mental health treatment in past 12 months	902 (10.6)	77 (6.4)	78 (10.1)	41 (6.3)
Excess alcohol use[b] (%)				
No alcohol use	1979 (23.63)	277 (23.18)	183 (23.77)	150 (23.08)
Never	2882 (34.41)	312 (26.11)	254 (32.99)	259 (39.85)
<Monthly	2516 (30.04)	317 (26.53)	165 (21.43)	168 (25.85)
Monthly	688 (8.21)	166 (13.89)	80 (10.39)	47 (7.23)
Weekly or daily	310 (3.70)	123 (10.29)	88 (11.43)	26 (4.00)

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CFD, Chicago Fire Department; CFI, Cognitive Function Instrument; FDNY, Fire Department of the City of New York; HR QoL (SF-12), Health-Related Quality of Life Short Form 12; MCS, mental component summary; PCL-S, PTSD Checklist Specific; PCS, physical component summary; PFD, Philadelphia Fire Department; SFFD, San Francisco Fire Department; WTC, World Trade Center.

[a]Includes Asian, Pacific Islander, Hawaiian, Native American, and other/unknown race.

[b]Defined using participant responses to the question "In the past 12 months, how often have you had six or more drinks on one occasion?"

TABLE 2 Multivariable regression models with PTSD symptom scores as the outcome in male firefighters, by fire department

	WTC-exposed firefighters		Non-WTC-exposed firefighters					
	FDNY		CFD		PFD		SFFD	
Variable	β ± SE	p	β ± SE	p	β ± SE	p	β ± SE	p
Intercept	25.84±0.19	<.001	23.45±0.56	<.001	25.68±0.77	<.001	24.81±0.73	<.001
CFI score	2.93±0.04	<.001	1.99±0.09	<.001	2.30±0.12	<.001	1.78±0.12	<.001
Age at exam	−0.05±0.01	<.001	−0.12±0.03	<.001	−0.23±0.04	<.001	−0.14±0.04	<.001
Race/ethnicity								
Non-Hispanic Black versus Non-Hispanic White	0.75±0.60	.215	1.33±0.81	.099	−0.69±0.94	.461	−1.69±1.24	.176
Hispanic versus Non-Hispanic White	−0.53±0.51	.297	−1.15±0.71	.104	1.15±1.91	.545	0.27±0.96	.782
Other race[a] versus Non-Hispanic White	1.41±1.60	.380	2.37±1.10	.032	1.07±1.73	.538	0.09±0.85	.913
Education level								
Associates degree versus HS/some college	0.17±0.27	.530	1.22±0.65	.061	0.15±1.00	.878	−1.26±0.82	.124
Bachelor's degree versus HS/some college	−0.11±0.20	.566	0.60±0.54	.266	−0.29±0.92	.750	0.15±0.70	.830
Smoking status								
Former versus never	0.10±0.20	.625	0.78±0.51	.123	−0.12±0.72	.870	−0.08±0.71	.911
Current versus never	0.90±0.58	.123	0.81±0.91	.372	−1.12±1.22	.360	2.06±1.78	.249
Excess alcohol use[b]								
No alcohol use versus never	1.09±0.23	<.001	0.90±0.65	.166	2.33±0.88	.008	0.51±0.81	.528
<Monthly versus never	0.44±0.22	.047	−0.11±0.63	.861	−0.10±0.92	.911	0.47±0.79	.555
Monthly versus never	1.85±0.34	<.001	−0.80±0.76	.296	1.18±1.17	.313	−0.45±1.25	.720
Weekly/daily versus never	3.17±0.48	<.001	1.46±0.85	.086	1.60±1.14	.163	0.07±1.62	.968

Abbreviations: CFD, Chicago Fire Department; CFI, Cognitive Function Instrument; FDNY, Fire Department of the City of New York; PFD, Philadelphia Fire Department; PTSD, posttraumatic stress disorder; SFFD, San Francisco Fire Department; WTC, World Trade Center.

[a]Includes Asian, Pacific Islander, Hawaiian, Native American, and other/unknown race.

[b]Defined using participant responses to the question "In the past 12 months, how often have you had six or more drinks on one occasion?"

TABLE 3 Multivariable regression models with depressive symptom scores as the outcome in male firefighters, by fire department

	WTC-exposed firefighters		Non-WTC-exposed firefighters					
	FDNY		CFD		PFD		SFFD	
Variable	β ± SE	p	β ± SE	p	β ± SE	p	β ± SE	p
Intercept	9.05±0.16	<.001	7.32±0.47	<.001	9.38±0.59	<.001	8.42±0.65	<.001
CFI score	2.41±0.03	<.001	1.79±0.08	<.001	1.98±0.09	<.001	1.67±0.10	<.001
Age at exam	−0.02±0.01	.040	−0.10±0.02	<.001	−0.18±0.03	<.001	−0.07±0.03	.031
Race/ethnicity								
Non-Hispanic Black versus Non-Hispanic White	−0.14±0.51	.778	0.08±0.67	.902	−1.68±0.72	.021	−1.18±1.10	.282
Hispanic versus Non-Hispanic White	−0.51±0.43	.240	−0.16±0.59	.788	−1.24±1.47	.401	0.58±0.85	.496
Other race[a] versus Non-Hispanic White	0.90±1.36	.509	0.94±0.92	.308	2.22±1.33	.097	0.67±0.75	.370
Education level								
Associates degree versus HS/some college	−0.03±0.23	.889	0.33±0.54	.546	0.22±0.77	.776	0.74±0.72	.302
Bachelor's degree versus HS/some college	−0.14±0.17	.390	0.26±0.45	.565	−0.19±0.71	.791	0.18±0.62	.768
Smoking status								
Former versus never	0.29±0.17	.078	0.91±0.42	.033	0.08±0.55	.884	0.17±0.62	.788
Current versus never	1.43±0.49	.004	2.24±0.76	.003	0.47±0.94	.616	2.46±1.57	.119
Excess alcohol use[b]								
No alcohol use versus never	1.09±0.20	<.001	1.50±0.54	.006	1.13±0.67	.096	0.12±0.71	.868
<Monthly versus never	0.53±0.19	.004	−0.22±0.53	.683	−1.34±0.71	.059	−0.53±0.69	.444
Monthly versus never	1.54±0.29	<.001	0.35±0.64	.581	−0.54±0.91	.552	0.16±1.11	.887
Weekly/daily versus never	2.84±0.41	<.001	0.87±0.71	.220	−0.02±0.88	.981	0.28±1.43	.844

Abbreviations: CFD, Chicago Fire Department; CFI, Cognitive Function Instrument; FDNY, Fire Department of the City of New York; PFD, Philadelphia Fire Department; SFFD, San Francisco Fire Department; WTC, World Trade Center.

[a]Includes Asian, Pacific Islander, Hawaiian, Native American, and other/unknown race.

[b]Defined using participant responses to the question "In the past 12 months, how often have you had six or more drinks on one occasion?"

TABLE 4 Multivariable regression models with subjective cognitive concerns as the outcome in male firefighters, by fire department

	WTC-exposed firefighters		Non-WTC-exposed firefighters					
	FDNY		CFD		PFD		SFFD	
Variable	β ± SE	p	β ± SE	p	β ± SE	p	β ± SE	p
Intercept	1.35±0.04	<.001	1.81±0.15	<.001	2.04±0.19	<.001	1.88±0.21	<.001
CES-D score	0.18±0.002	<.001	0.18±0.01	<.001	0.20±0.01	<.001	0.17±0.01	<.001
Age at exam	0.01±0.003	<.001	0.03±0.01	<.001	0.05±0.01	<.001	0.02±0.01	.158
Race/ethnicity								
Non-Hispanic Black versus Non-Hispanic White	0.22±0.14	.107	−0.09±0.21	.680	0.01±0.23	.962	0.21±0.35	.558
Hispanic versus Non-Hispanic White	0.30±0.12	.009	0.06±0.19	.761	0.43±0.46	.354	−0.19±0.27	.480
Other race[a] versus Non-Hispanic White	0.06±0.37	.875	0.42±0.29	.148	−0.17±0.42	.687	0.06±0.24	.787
Education level								
Associates degree versus HS/some college	0.01±0.06	.817	−0.02±0.17	.894	−0.19±0.24	.432	0.01±0.23	.982
Bachelor's degree versus HS/some college	−0.13±0.04	.004	−0.02±0.14	.916	0.22±0.22	.335	−0.23±0.20	.246
Smoking status								
Former versus never	0.02±0.04	.684	0.14±0.13	.288	−0.09±0.17	.624	0.26±0.20	.202
Current versus never	−0.05±0.13	.685	0.09±0.24	.694	−0.06±0.30	.832	−0.55±0.51	.280
Excess alcohol use[b]								
No alcohol use versus never	0.19±0.05	.001	0.24±0.17	.158	−0.02±0.21	.924	0.34±0.23	.140
<Monthly versus never	0.01±0.05	.853	0.09±0.17	.603	0.49±0.22	.030	0.06±0.22	.798
Monthly versus never	0.04±0.08	.594	0.16±0.20	.436	0.34±0.28	.235	0.04±0.35	.905
Weekly/daily versus never	0.32±0.11	.004	0.48±0.22	.032	0.48±0.28	.081	0.44±0.46	.344

Abbreviations: CFD, Chicago Fire Department; CFI, Cognitive Function Instrument; FDNY, Fire Department of the City of New York; PFD, Philadelphia Fire Department; SFFD, San Francisco Fire Department; WTC, World Trade Center.

[a]Includes Asian, Pacific Islander, Hawaiian, Native American, and other/unknown race.

[b]Defined using participant responses to the question "In the past 12 months, how often have you had six or more drinks on one occasion?"

TABLE 5 Multivariable regression models assessing the association between WTC exposure and CFI scores in male firefighters

	CFI score		CFI score	
Variable	β ± SE	p	β ± SE	p
Intercept	2.44±0.08	<.001	2.03±0.07	<.001
WTC exposure	−0.76±0.06	<.001	−0.69±0.05	<.001
Age at exam	0.02±0.003	<.001	0.02±0.002	<.001
Race/ethnicity				
Non-Hispanic Black versus non-Hispanic White	0.06±0.12	.628	0.11±0.09	.255
Hispanic versus non-Hispanic White	0.14±0.11	.224	0.12±0.09	.185
Other race[a] versus non-Hispanic White	0.43±0.17	.012	0.06±0.13	.648
Education level				
Some college versus HS	−0.15±0.07	.029	−0.02±0.05	.716
Associates degree versus HS	−0.13±0.09	.148	−0.02±0.07	.787
Bachelor's degree versus HS	−0.42±0.07	<.001	−0.13±0.06	.022
CES-D score			0.18±0.002	<.001
Smoking status				
Former versus never			0.05±0.04	.202
Current versus never			−0.05±0.10	.654
Excess alcohol use[b]				
No alcohol use versus never			0.19±0.05	<.001
<Monthly versus never			0.04±0.05	.398
Monthly versus never			0.07±0.07	.314
Weekly/daily versus never			0.37±0.09	<.001

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; CFI, Cognitive Function Instrument; WTC, World Trade Center.

[a]Includes Asian, Pacific Islander, Hawaiian, Native American, and other/unknown race.

[b]Defined using participant responses to the question "In the past 12 months, how often have you had six or more drinks on one occasion?"

Comparing self-reported obstructive airway disease in firefighters with and without World Trade Center exposure

Alexandra K. Mueller, MPH; Ankura Singh, MPH; Mayris P. Webber, DrPH; Charles B. Hall, PhD; David J. Prezant, MD; Rachel Zeig-Owens, DrPH

Introduction

Firefighting has long been associated with adverse respiratory effects.[1-5] During the course of a fire response, firefighters encounter various combustion byproducts including some known respiratory toxins.[6,7] Specifically, exposure to these toxins in fire settings has been associated with upper and lower respiratory symptoms, increased airway responsiveness, decreased pulmonary function, and diagnoses of obstructive airway disease (OAD).[1,3-5,8-12]

The attack on the World Trade Center (WTC) on 9/11/2001 (9/11) exposed rescue/recovery workers to a massive dust cloud containing many known respiratory hazards.[13] Since then, exposed firefighters from the Fire Department of the City of New York (FDNY) have had increased occurrences of airway hyperreactivity, bronchial wall thickening, rapid lung function decline,[14-16] and OAD diagnoses including asthma and chronic obstructive pulmonary disease (COPD).[15,17-19]

Since WTC-exposed firefighters have also encountered more typical firefighting hazards during their careers, current WTC research has not adequately controlled for the potentially confounding variable of the firefighting occupation.[15,17-20] The present study was undertaken to assess whether WTC-exposed firefighters have a greater risk of self-reported OAD diagnoses compared with non-WTC-exposed firefighters using data from the Career Firefighter Health Study (CFHS) cohort, which is comprised of career firefighters from the New York City, Chicago, Philadelphia, and San Francisco Fire Departments.[21] Additionally, to provide context for our findings, firefighters from each group (WTC-exposed and non-WTC-exposed) were compared with the general population using data from the National Health Interview Survey (NHIS).

Methods

Study population

Firefighters from the Career Firefighter Health Study who were actively employed by their respective fire departments on 9/11, completed a self-administered health questionnaire, and provided written informed consent were included in the study's source population (n=13,443). The study population was comprised of two firefighter groups: a WTC-exposed and a non-WTC-exposed group.

FDNY WTC-exposed group

Firefighters employed by FDNY who performed rescue/recovery work at the WTC disaster site were considered WTC-exposed. Of the 9,929 in the source population, we excluded: 115 firefighters who arrived at the WTC disaster site after 9/24/2001, 20 female firefighters, and three whose only health questionnaire date was after May 26, 2021, the latest questionnaire date in the non-WTC-exposed firefighter comparison cohort. The final analytic population was 9,791.

Non-WTC-exposed firefighter group

Using an FDNY non-WTC-exposed group was not possible, as few who were actively employed on 9/11 were unexposed (n=167), mostly due to pre-9/11 health issues. Instead, the non-WTC-exposed firefighter comparison population was comprised of career firefighters from fire departments in Chicago, Philadelphia, and San Francisco, whose roster information was originally obtained by the National Institute for Occupational Safety and Health (NIOSH).[22] A subset of this population was alive and eligible for follow-up, as described elsewhere.[21] A subset of eligible non-FDNY members completed a self-administered health questionnaire similar to the FDNY health monitoring questionnaire by May 26, 2021 (n=3,346). Respondents were demographically similar to non-respondents.[21] We excluded 208 female firefighters and 283 firefighters who reported WTC exposure. The final analytic population was 2,855.

U.S. general population

Additionally, for an overall comparison, we used the 2019 NHIS cross-sectional household interview survey of the US noninstitutionalized civilian population from all 50 states conducted by the National Center for Health Statistics.[23] The study was approved by the Montefiore Medical Center/Albert Einstein College of Medicine Institutional Review Board.

Demographic and other information

WTC-exposed firefighters' demographic data and last medical monitoring exam date were available from FDNY databases. WTC exposure was self-reported by FDNY participants at their first post-9/11 health questionnaire.[24] WTC exposure was defined according to participants' time of initial arrival at the WTC site. During their first post-9/11 medical monitoring examination, participants indicated whether they had arrived at the site on the morning of 9/11, the afternoon

of 9/11, anytime on 9/12/2001, or between 9/ 13–9/24/2001. Non-WTC-exposed firefighter demographic data were obtained from fire department records. Non-WTC-exposed firefighters reported length of time since their last medical visit on their health questionnaire, which was dichotomized as within the past two years or more than two years. For WTC-exposed firefighters, health surveys were taken at the time of their routine FDNY medical monitoring exam. Therefore, time between the survey date (i.e., last exam) and the penultimate exam was calculated and similarly dichotomized. Firefighters self-reported smoking status as former, current, or never smokers. Former or current smokers were considered "ever smokers."

Self-reported OAD diagnoses

The FDNY questionnaire is given during WTC-exposed participants' routine medical monitoring exams. A self-reported OAD diagnosis at the most recent questionnaire was based on a positive response to the question, "In the past 12 months, has a doctor or health professional told you that you had any of the following? 1. Asthma; 2. Emphysema or COPD; 3. Bronchitis." The non-WTC-exposed firefighter questionnaire has been taken only once and asks about "ever" diagnoses of OAD. A self-reported OAD diagnosis was based on a positive response to the question, "Has a doctor or health professional ever told you have you had any of the following problems? 1. Asthma; 2. Emphysema; 3. COPD; 4. Bronchitis." To obtain an appropriate "ever" comparison in the WTC-exposed cohort, we combined all prior FDNY questionnaire information. For both cohorts, self-reported diagnoses were categorized as (1) self-reported asthma, (2) self-reported emphysema, chronic bronchitis, or other non-specific COPD, henceforth referred to as "COPD", and (3) self-reported any OAD which included reporting either of the two conditions.

Both questionnaires obtained respondents' medication use in the past 12 months. These multiple-choice questions allowed participants to select antibiotics, inhaled bronchodilators, inhaled or oral corticosteroids, montelukast, nebulized bronchodilators, and/or other. A positive answer to any of the medications listed was classified as "any OAD medication." In sensitivity analyses, stricter case definitions were used for OAD; those with any self-reported outcome (any OAD, asthma, or COPD) *and* any OAD medication in the past 12 months were re-classified as "treated any OAD," "treated asthma," or "treated COPD." Those who reported an outcome but were not on medication in the past 12 months were re-classified as "untreated."

National Health Interview Survey data

The 2019 version of the NHIS was chosen because the health questions were the most similar to the firefighter questionnaires. Data from NHIS participants were restricted to males aged 35+ years who did not reside in the South to be most comparable to the firefighter populations. NHIS participants reported their birth date, residence by region, race/ethnicity, smoking status, and length of time since their last medical visit (also dichotomized as ≤2 years/>2 years). They also answered the questions, "Have you ever been told by a doctor or other health professional that you had asthma?" and "Have you ever been told by a doctor or other health professional that you had Chronic Obstructive Pulmonary Disease, COPD, emphysema, or chronic bronchitis?" A positive answer to either of these questions was classified as "any OAD." All diagnoses in this study are self-reported and henceforth will be referred to as asthma, COPD, and OAD.

Statistical analysis

Demographic and other characteristics were represented as proportions (%) and means (±SD) for the firefighter groups.

Among all firefighters, multivariable logistic regression was used to estimate the associations between WTC exposure (exposed/non-exposed) and diagnoses of any OAD, asthma, and COPD as binary variables (ever/never diagnosed). Models controlled for age, race, ever-smoking, and having a last medical visit within the past two years. We assessed interaction between WTC exposure and smoking status; models with significant interaction terms were stratified by smoking status. In secondary analyses, WTC-exposure level was assessed with the earliest arrival time considered as the highest intensity exposure and the non-WTC-exposed as the reference. We conducted a trend test to assess if there is an exposure gradient of arrival time and OAD.

Multivariable logistic regression was also used to estimate associations between the firefighting occupation and OAD diagnoses. First, all firefighters were compared with general population data from the 2019 NHIS while controlling for age, race, ever-smoking, and having a last medical visit within the past two years. Second, the WTC-exposed and non-WTC-exposed groups were compared with the general population, while controlling for the above covariates.

We conducted three sensitivity analyses where the above multivariable logistic regression analyses were repeated using stricter case definitions of OAD. The first sensitivity analysis estimated the association between WTC exposure and treated OAD (asthma, COPD, or any OAD). WTC-exposed firefighters with missing medication data were excluded from

these analyses (n=68). The second sensitivity analysis addressed potential detection bias due to differential case ascertainment. Only those in the WTC-exposed group who reported an asthma or COPD diagnosis on >50% of the surveys they completed after an initial self-report of the diagnosis were considered to have a positive diagnosis. The third addressed asthma-COPD overlap syndrome, an endotype of COPD seen in WTC responders,[25-27] by estimating associations between WTC exposure and an isolated diagnosis of asthma, an isolated diagnosis of COPD, and both asthma and COPD diagnoses (possible asthma/COPD overlap syndrome). All data analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, http://www.sas.com).

Results

Characteristics describing the 9,792 WTC-exposed and 3,138 non-WTC-exposed firefighters are displayed in Table I. WTC-exposed firefighters were, on average, slightly younger, less likely to report ever smoking, and more likely to be white than non-WTC-exposed firefighters. A greater proportion of WTC-exposed firefighters reported ever being diagnosed with asthma and COPD (which includes diagnoses of emphysema, chronic bronchitis, or other non-specific COPD) as well as taking OAD-related medication in the year prior to their questionnaire date. The majority of both cohorts reported a medical visit within two years of their questionnaire, and, among those with a diagnosis of any OAD, both groups report similar rates of medication use.

OAD diagnoses in WTC-exposed vs. non-WTC-exposed firefighters

We observed an association between WTC exposure and any OAD diagnosis (OR=4.48; 95% CI: 4.03, 4.98) after controlling for age, race, ever smoking, and last medical visit within two years (Figure 1; Table S1 shows the full models with covariates). Odds of asthma were over six times greater in WTC-exposed (OR=6.31; 95% CI: 5.41, 7.37) after controlling for the above covariates. There was evidence of effect modification by smoking status when assessing the association between WTC exposure and COPD (*p* for interaction <0.001); accordingly, the analyses were stratified by smoking status (Table S2). Among never smokers, WTC-exposed firefighters had elevated odds of COPD (OR=5.27; 95% CI: 4.47, 6.21) when compared with non-exposed firefighters. Among ever smokers, odds of COPD were also greater in WTC-exposed firefighters, though to a lesser extent than in never smokers (OR=3.26; 95% CI: 2.77, 3.84). When including WTC-exposure intensity in the model, we observed an exposure gradient with those arriving earlier having higher odds of any OAD (p<0.0001), asthma (p<0.0001), and COPD in both smokers (p=0.03) and non-smokers (p=0.003) (data not shown).

OAD diagnoses in firefighters vs. general population

Odds of any OAD diagnosis were over five times greater in firefighters compared with general population males aged 35 years and older (OR=5.53; 95% CI: 5.13, 5.97) after adjusting for age, race, ever smoking, and last medical visit within two years (Table II). A separate model in which firefighters were classified as WTC-exposed or non-WTC-exposed also showed associations between firefighting group and any OAD, with WTC-exposed firefighters having over 7 times greater odds compared with general population (OR=7.73; 95% CI: 7.14, 8.37) and non-WTC exposed firefighters having 1.68 times greater odds (OR=1.68; 95% CI: 1.50, 1.88). Associations between firefighting and COPD followed a similar pattern, both for ever smokers and never smokers (Table II).

Similar to the other diagnoses, odds of asthma were greater in all firefighters and WTC-exposed firefighters compared with the general population after adjusting for covariates. However, non-WTC-exposed firefighters had about 30% *lower* odds of asthma than the general population (OR=0.69; 95% CI: 0.60, 0.81) (Table II).

The first sensitivity analysis examined the association between WTC exposure and treated OAD. Table I includes the proportion of firefighters with treated OAD by WTC exposure. Among all firefighters who reported any OAD, 58% in WTC-exposed and 64% in non-exposed reported treatment with respiratory medications within the past year. Logistic regression analyses estimated the odds of having any treated OAD to be greater in WTC-exposed vs. non-WTC-exposed (OR=2.88; 95% CI: 2.55, 3.26), controlling for covariates. Treated asthma and treated COPD were also significantly higher in WTC-exposed compared with the non-exposed (Table S3).

The second sensitivity analysis estimated the association between WTC exposure and OAD with WTC-exposed firefighters being considered to have asthma or COPD only if they reported the diagnosis on >50% of surveys after the first instance reporting said diagnosis (consistent). The odds of having asthma remained greater in those who were WTC-exposed (OR=3.21; 95% CI: 2.74, 3.76). Among ever smokers, odds of consistent COPD were 24% lower in the WTC-exposed firefighters compared to the non-exposed (OR=0.76; 95% CI: 0.64, 0.91) (Table S4). There was no association among never smokers. The third sensitivity analysis estimated the associations between WTC exposure and those reporting only asthma, only COPD, and those reporting both (asthma/COPD overlap) diagnoses. Associations between WTC exposure and only asthma or COPD were attenuated compared to the associations observed in the main analysis, but

still significant (Table S5). Odds of asthma/COPD overlap were over 12 times greater in WTC-exposed compared with non-WTC-exposed firefighters (OR=12.22; 95% CI: 9.56, 15.62).

Discussion

This study is the first to compare OAD in WTC-exposed responders to an appropriate, non-WTC-exposed occupational cohort. This allowed us to draw conclusions about the impact WTC rescue/recovery work had on respiratory outcomes while controlling for the potentially confounding variable of firefighting occupation. We found that WTC exposure was strongly associated with increased odds of all OAD after controlling for age, race, smoking status, and last medical visit within two years. The association was particularly strong for asthma diagnoses, which were over six times greater among WTC-exposed. Results for COPD were stratified by ever smokers and never smokers due to effect modification by smoking status. For both smoking groups, WTC exposure was associated with greater odds of COPD, with a stronger association in never smokers. In sensitivity analyses using more stringent case criteria, associations between WTC exposure and diagnoses of OAD remained statistically significant.

Prior research on WTC responders has shown associations between WTC exposure and OAD.[15,18,24,28-30] In this study, we set out to estimate the additional burden of WTC exposure on top of routine firefighting because it is well-established that firefighting in general also increases the risk of adverse respiratory OAD outcomes it is essential to control for this potential confounder in order to improve causal inference.[1,3-5,8-10] We found that WTC-exposed firefighters had greater odds of any OAD diagnosis, asthma, and COPD compared with non-WTC-exposed firefighters. Specifically, the odds of COPD, in ever smokers and never smokers, and asthma were between three- to six-fold higher in WTC-exposed firefighters compared with the non-WTC-exposed. Additionally, we observed an exposure gradient where earlier arrival to the WTC site is associated with greater reporting of any OAD. This concurs with the current literature that shows high and sustained prevalence of asthma and COPD, which included bronchitis and emphysema, among FDNY WTC-exposed firefighters.[15,18,25,31,32]

We were also interested in evaluating the concomitant association between firefighting with or without WTC exposure and OAD to assess the relationship of each factor. Studies have found that firefighters have increased risk of asthma compared to military employees and police officers.[10,33] In our study, a comparison with the general US population showed an association between firefighting and any OAD diagnosis, with strongest associations found among WTC-exposed firefighters.

The odds of asthma were over 4-fold greater in WTC-exposed firefighters compared to the general population. Conversely, non-WTC-exposed firefighters had 30% *lower* odds of asthma compared with the general population – a finding that we believe is attributable to the healthy worker effect.[34-37] US fire departments, including these four, exclude candidate firefighters that have previously been diagnosed with asthma to ensure they will be able to safely and effectively do the job.[38] As such, observing reduced odds of asthma in non-WTC-exposed firefighters compared with the general population could be attributable to this hiring practice and to their retention in the workforce. This is also what makes the intensity of the WTC exposure signal interesting: our findings suggest that the effect of WTC exposure on OAD diagnoses, asthma especially, exists despite the healthy worker effect. These findings highlight the importance of having a firefighter comparison population for WTC-related health studies as opposed to relying on the general population.

A general population comparison is helpful, however, when comparing the extent of the WTC effect on OAD with that of the firefighting effect. When comparing all firefighters to the general population, we found the association between firefighting and OAD diagnoses was particularly strong for COPD (which includes diagnoses of emphysema, chronic bronchitis, or other non-specific COPD). However, while we observed the health worker effect with non-WTC firefighting and asthma, the same was not found for COPD, which demonstrates an increased risk for COPD in career firefighters without WTC exposure. This is consistent with a recent review finding that the association between firefighting and COPD was greatest for those reporting acute severe firefighting exposures.[12] Prior reports of firefighter prevalence of COPD vary greatly, but there is evidence to suggest that firefighting nearly doubles the prevalence of chronic bronchitis specifically.[8,39,40] Our results suggest that while WTC exposure is associated with COPD, being a career firefighter also increases risk – a risk that may be even greater for never smokers than for ever smokers. This builds upon our prior work comparing chronic bronchitis among WTC-exposed firefighters to the general population.[19]

There are limitations to this investigation. The use of self-reported outcomes is subject to measurement/recall bias. However, our large prior study in the WTC-exposed firefighter cohort found good agreement between self-reported diagnoses of OAD and electronic medical record data – with 92% agreement for asthma.[19] Sensitivity analyses conducted to account for potential overreporting by requiring OAD medication use found somewhat attenuated, but essentially

similar results to the primary analyses. Another limitation is that the WTC-exposed firefighters included in this study are all enrolled in the WTC Health Program, which provides no-cost annual medical monitoring and treatment for certified health conditions, as well as with education regarding their diagnoses. Within this rigorous program, WTC-exposed firefighters are highly encouraged to complete an annual medical exam and survey, which may lead to higher case ascertainment; the non-WTC-exposed firefighters only completed the surveys once. To account for this, we controlled for having a last medical visit within two years in the model. Both WTC-exposed and non-WTC-exposed firefighters reported a high and similar proportion of a last medical visit within the past two years, 93% and 95%, respectively. To account for the differential opportunity for diagnosis reporting between the cohorts, another sensitivity analysis restricted OAD outcomes for WTC-exposed firefighters to those who reported the diagnosis on most surveys. Compared with the primary analysis, odds of asthma were attenuated, but still significantly greater for the WTC-exposed versus the non-exposed firefighters. There was an inverse association between WTC exposure and COPD in ever smokers and no association in never smokers. This may be due to severity of the diagnoses or individual differences in physician diagnostic criteria; physicians may be more likely to attribute lower airway symptoms to OAD if a patient was exposed to the WTC disaster. Our study did not include medical record reviews to confirm the presence or absence of self-reported diagnoses. Additionally, unmeasured confounding could have biased our results; for example, we did not have access to occupation data from the 2019 NHIS. However, <1% of the male population in the US in 2019 was a career firefighter.[41] Lastly, there could be potential differences in routine occupational exposure between firefighters in New York City compared with the other cities. Given the size of the observed effect estimates, it is unlikely that these additional confounding variables would have changed the direction of the association and more likely would only have affected its magnitude.

This study has numerous strengths. It is the first to compare respiratory diagnoses in WTC rescue/recovery workers to diagnoses in a comparison population having the same occupation, in this case career urban firefighting. Being able to control for the firefighting occupation, a confounding variable, allows for a clearer understanding of the association between WTC exposure and OAD. The sample size is also among the largest of firefighter comparison studies currently published.

We found that firefighters who responded to the WTC disaster carry a disproportionately high burden of disease. WTC-exposed firefighters had greater odds of any OAD diagnoses compared with both non-WTC-exposed firefighters and the general population. Firefighters without WTC exposure had higher rates of COPD, but not asthma, compared with the general population. Future studies that examine the symptom severity and persistence of OAD will be useful in understanding the lasting effect that firefighting with and without WTC exposure can have on respiratory health and disease progression.

References

1. Gaughan DM, Cox-Ganser JM, Enright PL, et al. Acute upper and lower respiratory effects in wildland firefighters. J Occup Environ Med. 2008;50(9):1019-28. Epub 2008/09/12. doi: 10.1097/JOM.0b013e3181754161. PubMed PMID: 18784550.

2. Greven FE, Krop EJ, Spithoven JJ, et al. Acute respiratory effects in firefighters. Am J Ind Med. 2012;55(1):54-62. Epub 2011/10/01. doi: 10.1002/ajim.21012. PubMed PMID: 21959832.

3. Greven FE, Rooyackers JM, Kerstjens HA, Heederik DJ. Respiratory symptoms in firefighters. Am J Ind Med. 2011;54(5):350-5. Epub 2011/01/20. doi: 10.1002/ajim.20929. PubMed PMID: 21246589.

4. Liu D, Tager IB, Balmes JR, Harrison RJ. The effect of smoke inhalation on lung function and airway responsiveness in wildland fire fighters. Am Rev Respir Dis. 1992;146(6):1469-73. Epub 1992/12/01. doi: 10.1164/ajrccm/146.6.1469. PubMed PMID: 1456562.

5. Sherman CB, Barnhart S, Miller MF, et al. Firefighting acutely increases airway responsiveness. Am Rev Respir Dis. 1989;140(1):185-90. Epub 1989/07/01. doi: 10.1164/ajrccm/140.1.185. PubMed PMID: 2665585.

6. Baxter CS, Hoffman JD, Knipp MJ, Reponen T, Haynes EN. Exposure of firefighters to particulates and polycyclic aromatic hydrocarbons. J Occup Environ Hyg. 2014;11(7):D85-91. Epub 2014/02/12. doi: 10.1080/15459624.2014.890286. PubMed PMID: 24512044; PMCID: PMC4653736.

7. Brandt-Rauf PW, Fallon LF, Jr., Tarantini T, Idema C, Andrews L. Health hazards of fire fighters: exposure assessment. Br J Ind Med. 1988;45(9):606-12. Epub 1988/09/01. doi: 10.1136/oem.45.9.606. PubMed PMID: 3179235; PMCID: PMC1009663.

8. Betchley C, Koenig JQ, van Belle G, Checkoway H, Reinhardt T. Pulmonary function and respiratory symptoms in forest firefighters. Am J Ind Med. 1997;31(5):503-9. Epub 1997/05/01. doi: 10.1002/(sici)1097-0274(199705)31:5<503::aid-ajim3>3.0.co;2-u. PubMed PMID: 9099351.
9. Choi JH, Shin JH, Lee MY, Chung IS. Pulmonary function decline in firefighters and non-firefighters in South Korea. Ann Occup Environ Med. 2014;26:9. Epub 2014/05/06. doi: 10.1186/2052-4374-26-9. PubMed PMID: 24795815; PMCID: PMC4009061.
10. Ribeiro M, de Paula Santos U, Bussacos MA, Terra-Filho M. Prevalence and risk of asthma symptoms among firefighters in Sao Paulo, Brazil: a population-based study. Am J Ind Med. 2009;52(3):261-9. Epub 2009/01/01. doi: 10.1002/ajim.20669. PubMed PMID: 19117017.
11. Schermer TR, Malbon W, Morgan M, Smith M, Crockett AJ. Chronic respiratory conditions in a cohort of metropolitan fire-fighters: associations with occupational exposure and quality of life. Int Arch Occup Environ Health. 2014;87(8):919-28. Epub 2014/02/27. doi: 10.1007/s00420-014-0935-8. PubMed PMID: 24570328.
12. Rajnoveanu AG, Rajnoveanu RM, Motoc NS, Postolache P, Gusetu G, Man MA. COPD in Firefighters: A Specific Event-Related Condition Rather than a Common Occupational Respiratory Disorder. Medicina (Kaunas). 2022;58(2). Epub 2022/02/26. doi: 10.3390/medicina58020239. PubMed PMID: 35208563; PMCID: PMC8878660.
13. Lioy PJ, Weisel CP, Millette JR, et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. Environ Health Perspect. 2002;110(7):703-14. Epub 2002/07/16. doi: 10.1289/ehp.02110703. PubMed PMID: 12117648; PMCID: PMC1240917.
14. Aldrich TK, Weakley J, Dhar S, et al. Bronchial Reactivity and Lung Function After World Trade Center Exposure. Chest. 2016;150(6):1333-1340. Epub 2016/07/23. doi: 10.1016/j.chest.2016.07.005. PubMed PMID: 27445092; PMCID: PMC6026231.
15. Weiden MD, Ferrier N, Nolan A, et al. Obstructive airways disease with air trapping among firefighters exposed to World Trade Center dust. Chest. 2010;137(3):566-74. Epub 2009/10/13. doi: 10.1378/chest.09-1580. PubMed PMID: 19820077; PMCID: PMC2832867.
16. Banauch GI, Hall C, Weiden M, et al. Pulmonary function after exposure to the World Trade Center collapse in the New York City Fire Department. Am J Respir Crit Care Med. 2006;174(3):312-9. Epub 2006/04/29. doi: 10.1164/rccm.200511-1736OC. PubMed PMID: 16645172; PMCID: PMC2648115.
17. Glaser MS, Webber MP, Zeig-Owens R, et al. Estimating the time interval between exposure to the World Trade Center disaster and incident diagnoses of obstructive airway disease. Am J Epidemiol. 2014;180(3):272-9. Epub 2014/07/02. doi: 10.1093/aje/kwu137. PubMed PMID: 24980522; PMCID: PMC4108044.
18. Hall CB, Liu X, Zeig-Owens R, et al. The Duration of an Exposure Response Gradient between Incident Obstructive Airways Disease and Work at the World Trade Center Site: 2001-2011. PLoS Curr. 2015;7. Epub 2015/06/13. doi: 10.1371/currents.dis.8a93e7682624698558a76a1fa8c5893f. PubMed PMID: 26064784; PMCID: PMC4449208.
19. Weakley J, Webber MP, Gustave J, et al. Trends in respiratory diagnoses and symptoms of firefighters exposed to the World Trade Center disaster: 2005-2010. Prev Med. 2011;53(6):364-9. Epub 2011/09/21. doi: 10.1016/j.ypmed.2011.09.001. PubMed PMID: 21930151.
20. Brackbill RM, Hadler JL, DiGrande L, et al. Asthma and posttraumatic stress symptoms 5 to 6 years following exposure to the World Trade Center terrorist attack. JAMA. 2009;302(5):502-16. Epub 2009/08/06. doi: 10.1001/jama.2009.1121. PubMed PMID: 19654385.
21. Zeig-Owens R, Singh A, Triplett S, et al. Assembling the Career Firefighter Health Study cohort: A methods overview. Am J Ind Med. 2021;64(8):680-687. Epub 2021/06/12. doi: 10.1002/ajim.23266. PubMed PMID: 34114224.
22. Daniels RD, Kubale TL, Yiin JH, et al. Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950-2009). Occup Environ Med. 2014;71(6):388-97. Epub 2013/10/22. doi: 10.1136/oemed-2013-101662. PubMed PMID: 24142974; PMCID: PMC4499779.
23. Centers for Disease Control and Prevention. About the National Health Interview Survey. Accessed May 4, 2022, https://www.cdc.gov/nchs/nhis/about_nhis.htm
24. Aldrich TK, Vossbrinck M, Zeig-Owens R, et al. Lung Function Trajectories in World Trade Center-Exposed New York City Firefighters Over 13 Years: The Roles of Smoking and Smoking Cessation. Chest. 2016;149(6):1419-27. Epub 2016/02/03. doi: 10.1016/j.chest.2015.10.067. PubMed PMID: 26836912; PMCID: PMC6026237.
25. Singh A, Liu C, Putman B, et al. Predictors of Asthma/COPD Overlap in FDNY Firefighters With World Trade Center Dust Exposure: A Longitudinal Study. Chest. 2018;154(6):1301-1310. Epub 2018/07/22. doi: 10.1016/j.chest.2018.07.002. PubMed PMID: 30028968; PMCID: PMC6289858.

26. Christenson SA, Steiling K, van den Berge M, et al. Asthma-COPD overlap. Clinical relevance of genomic signatures of type 2 inflammation in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2015;191(7):758-66. Epub 2015/01/23. doi: 10.1164/rccm.201408-1458OC. PubMed PMID: 25611785; PMCID: PMC4407484.
27. Cosentino J, Zhao H, Hardin M, et al. Analysis of Asthma-Chronic Obstructive Pulmonary Disease Overlap Syndrome Defined on the Basis of Bronchodilator Response and Degree of Emphysema. Ann Am Thorac Soc. 2016;13(9):1483-9. Epub 2016/06/09. doi: 10.1513/AnnalsATS.201511-761OC. PubMed PMID: 27268723; PMCID: PMC5614769.
28. Aldrich TK, Gustave J, Hall CB, et al. Lung function in rescue workers at the World Trade Center after 7 years. N Engl J Med. 2010;362(14):1263-72. Epub 2010/04/09. doi: 10.1056/NEJMoa0910087. PubMed PMID: 20375403; PMCID: PMC4940972.
29. Kim H, Herbert R, Landrigan P, et al. Increased rates of asthma among World Trade Center disaster responders. Am J Ind Med. 2012;55(1):44-53. Epub 2011/11/10. doi: 10.1002/ajim.21025. PubMed PMID: 22068920.
30. Zeig-Owens R, Singh A, Aldrich TK, et al. Blood Leukocyte Concentrations, FEV1 Decline, and Airflow Limitation. A 15-Year Longitudinal Study of World Trade Center-exposed Firefighters. Ann Am Thorac Soc. 2018;15(2):173-183. Epub 2017/11/04. doi: 10.1513/AnnalsATS.201703-276OC. PubMed PMID: 29099614; PMCID: PMC5802620.
31. Webber MP, Glaser MS, Weakley J, et al. Physician-diagnosed respiratory conditions and mental health symptoms 7-9 years following the World Trade Center disaster. Am J Ind Med. 2011;54(9):661-71. Epub 2011/10/04. doi: 10.1002/ajim.20993. PubMed PMID: 21966080; PMCID: PMC3181470.
32. Yip J, Webber MP, Zeig-Owens R, et al. FDNY and 9/11: Clinical services and health outcomes in World Trade Center-exposed firefighters and EMS workers from 2001 to 2016. Am J Ind Med. 2016;59(9):695-708. Epub 2016/07/19. doi: 10.1002/ajim.22631. PubMed PMID: 27427498.
33. Pedersen JE, Ugelvig Petersen K, Ebbehoj NE, Bonde JP, Hansen J. Risk of asthma and chronic obstructive pulmonary disease in a large historical cohort of Danish firefighters. Occup Environ Med. 2018;75(12):871-876. Epub 2018/10/17. doi: 10.1136/oemed-2018-105234. PubMed PMID: 30323012.
34. Radon K, Goldberg M, Becklake M. Healthy worker effect in cohort studies on chronic bronchitis. Scand J Work Environ Health. 2002;28(5):328-32. Epub 2002/11/16. doi: 10.5271/sjweh.682. PubMed PMID: 12432986.
35. Rosenstock L, Demers P, Heyer NJ, Barnhart S. Respiratory mortality among firefighters. Br J Ind Med. 1990;47(7):462-5. Epub 1990/07/01. doi: 10.1136/oem.47.7.462. PubMed PMID: 2383515; PMCID: PMC1035207.
36. Le Moual N, Kauffmann F, Eisen EA, Kennedy SM. The healthy worker effect in asthma: work may cause asthma, but asthma may also influence work. Am J Respir Crit Care Med. 2008;177(1):4-10. Epub 2007/09/18. doi: 10.1164/rccm.200703-415PP. PubMed PMID: 17872490; PMCID: PMC4767883.
37. McMichael AJ. Standardized mortality ratios and the "healthy worker effect": Scratching beneath the surface. J Occup Med. 1976;18(3):165-8. Epub 1976/03/01. doi: 10.1097/00043764-197603000-00009. PubMed PMID: 1255276.
38. Technical Committee of Fire Service Occupational Safety and Health. *NFPA 1582: Standard on Comprehensive Occupational Medical Program for Fire Departments.* 2006.
39. Ward BW, Nugent CN, Blumberg SJ, Vahratian A. Measuring the Prevalence of Diagnosed Chronic Obstructive Pulmonary Disease in the United States Using Data From the 2012-2014 National Health Interview Survey. Public Health Rep. 2017;132(2):149-156. Epub 2017/01/31. doi: 10.1177/0033354916688197. PubMed PMID: 28135423; PMCID: PMC5349479.
40. Mustajbegovic J, Zuskin E, Schachter EN, et al. Respiratory function in active firefighters. Am J Ind Med. 2001;40(1):55-62. Epub 2001/07/06. doi: 10.1002/ajim.1071. PubMed PMID: 11439397.
41. Fahy R, Evarts B, Stein GP. *US Fire Department Profile 2019*. December 2021.

Table I: Selected Population Characteristics

	WTC-exposed[1]	Non-WTC-exposed[2]
n	9791	2855
Mean age on 9/11 (SD)	40.2 (7.4)	44.1 (9.0)
Ever smokers	3223 (32.9%)	1192 (41.8%)

Last medical visit within 2 years	9093 (92.9%)	2709 (94.9%)
Race		
White	9218 (94.2%)	2051 (71.8%)
Black	236 (2.4%)	294 (10.3%)
Hispanic	308 (3.2%)	274 (9.6%)
Other[3]	29 (0.3%)	236 (8.27%)
Arrival time at WTC site		
Morning of 9/11	1597 (16.3%)	
Afternoon of 9/11	5280 (53.9%)	
Anytime on 9/12	1729 (17.7%)	
Anytime 9/13-9/24	1115 (12.1%)	
Self-reported diagnoses		
Any OAD[4]	5519 (56.4%)	625 (21.9%)
Asthma	3325 (34.0%)	215 (7.5%)
COPD	4543 (46.4%)	486 (17.0%)
Treated any OAD[5,6]	3165 (32.6%)	397 (13.9%)
Treated asthma[5,6]	2457 (25.3%)	166 (5.9%)
Treated COPD[5,6,7]	2566 (26.4%)	296 (10.4%)

[1]WTC-exposed firefighters from the New York City fire department
[2]Non-WTC-exposed firefighters from Chicago, Philadelphia, and San Francisco fire departments
[3]Includes Asian, Pacific Islander, Hawaiian, Native American, and other/unknown race
[4]Includes those who have a diagnosis of either asthma or COPD; n=2349 report a diagnosis of both
[5]Excludes 68 WTC-exposed firefighters who did not have available medication data
[6]Reported treatment with any breathing medications **in the year prior to taking the questionnaire** *and* having an OAD diagnosis
[7]Includes diagnoses of COPD, emphysema, and chronic bronchitis

II: Estimated odds ratios for self-reported OAD diagnoses by firefighter and exposure status

	All firefighters vs. NHIS[1,2]		WTC-exposed firefighters[1,3] vs. NHIS		Non-exposed firefighters[1,4] vs. NHIS	
	OR	95% CI	OR	95% CI	OR	95% CI
Any OAD	5.53	5.13, 5.97	7.73	7.14, 8.37	1.68	1.50, 1.88
Asthma	3.17	2.91, 3.45	4.26	3.90, 4.66	0.69	0.60, 0.81
COPD: Never smokers[5,6]	34.53	26.80, 44.50	46.07	35.67, 59.51	8.52	6.37, 11.39
COPD: Ever smokers[6,7]	6.41	5.65, 7.28	8.94	7.81, 10.22	2.52	2.11, 3.00

[1]Controlling for age, race, smoking status and last medical visit within 2 years
[2]National Health Interview Survey
[3]WTC-exposed firefighters from New York City
[4]Non-WTC-exposed firefighters from Chicago, Philadelphia, and San Francisco fire departments
[5]N=13,271
[6]Includes diagnoses of COPD, emphysema, and chronic bronchitis
[7]N=8,467

Self-reported cardiovascular disease in career firefighters with and without World Trade Center exposure

Alexandra K. Mueller, Hillel Cohen, DrPH, Ankura Singh, MPH, Mayris P. Webber, Charles B. Hall, PhD, David J. Prezant, MD, Rachel Zeig-Owens, DrPH

Introduction

On September 11, 2001 (9/11), the Fire Department of the City of New York (FDNY) firefighters and emergency medical service (EMS) providers were some of the first responders to the World Trade Center (WTC) disaster as their job tasks require them to respond to any emergency in New York City where their services might be required. Many FDNY firefighters and EMS providers, along with other rescue/recovery workers, continued work at the WTC disaster site for many months after 9/11. The WTC dust cloud included fine particulate matter,[1] which has been shown to be related to cardiovascular disease (CVD).[2,3] Approximately ten years after the disaster, researchers began to discover an association between rescue/recovery work at the WTC site and increased CVD risk.[4-8] Analyses of those enrolled in the WTC Health Registry, which includes WTC rescue/recovery workers and survivors, showed that WTC exposure may be a risk factor for self-reported heart disease or ischemic stroke.[5,8] In a cohort of general responders that included police officers, construction and communications workers, other skilled trades, and community volunteers, recent work suggests a dose-response relationship between arrival time to the WTC disaster site and CVD risk.[7] Similar results were found in a cohort of firefighters and EMS providers from FDNY, where age-adjusted incidence rates were higher for those with greater WTC exposure.[4]

However, other research has shown that firefighting alone may be independently associated with CVD. Aspects of firefighting, including physical and psychological stress,[9-12] shift work,[13] and exposures to smoke and other toxins,[14] have been linked to increased cardiovascular disease.[15] Current literature suggests a high prevalence of cardiovascular risk factors – hypertension (10-44%),[16-18] obesity (14-60%),[17,19,20] high cholesterol (20-57%),[17,21,22] and smoking (11-42%)[23-26] – within firefighters. Cardiac-related events have accounted for the largest proportion of on-duty firefighter fatalities (44%) since 2009,[27] and most occur in those with additional CVD risk factors.[15,28]

Previous research regarding the association of WTC exposure with CVD has not adequately accounted for potential confounding by the firefighting occupation.[4,6,7] The primary aim of this study was to assess whether WTC-exposed firefighters have greater odds of self-reported CVD diagnoses compared with non-WTC-exposed firefighters, using data from the Career Firefighter Health Study cohort, which is comprised of career firefighters from New York City, Chicago, Philadelphia, and San Francisco.[29] To provide context for our findings, firefighters were compared also with respondents of the National Health Interview Survey (NHIS) as a way of comparing with a general US population sample.

Methods

Study Population

This study's source population included WTC-exposed and non-WTC-exposed firefighters from the Career Firefighter Health Study who were actively employed on 9/11 by their respective fire departments (i.e., FDNY, Chicago Fire Department, Philadelphia Fire Department, or San Francisco Fire Department), completed a self-administered health questionnaire, and provided written informed consent (n=13,517). This study was approved by the Institutional Review Board of Albert Einstein College of Medicine/Montefiore Medical Center and follows STROBE guidelines (SDC-1).

WTC-Exposed Firefighters

Firefighters employed by FDNY who were alive at the start of administration of the non-WTC-exposed comparison cohort survey, February 16, 2019, were included in the study. Of the 10,095 in the source population, we excluded 128 firefighters who first arrived at the WTC site after 9/24/2001, 66 who were not exposed, 20 female firefighters, and 92 male firefighters who did not answer CVD-related questions on their health questionnaire. The final analytic WTC-exposed firefighter cohort was 9,789.

Non-WTC-Exposed Firefighters

As previously described,[30] using a non-WTC-exposed comparison group from FDNY was not possible due to small sample size (see above). Instead, we used data from non-WTC-exposed career firefighters from fire departments in Chicago, Philadelphia, and San Francisco whose roster information was originally obtained by the National Institute for Occupational Safety and Health (NIOSH).[31] A subset of this population was alive and eligible for follow-up, as described elsewhere.[29] Eligible non-FDNY members completed a self-administered health questionnaire similar to the FDNY health monitoring questionnaire between February 16, 2019 and May 26, 2021 (n=3,422). Respondents were demographically similar to non-respondents.[29] We excluded 329 non-FDNY firefighters who reported 9/11 exposure, 169 who did not provide a response to CVD questions, and 195 female firefighters. The final non-WTC-exposed firefighter cohort was 2,729.

WTC Exposure

Self-reported WTC exposure on FDNY participants' first post-9/11 health questionnaire was classified into high, moderate, and low exposure based on arrival time to the WTC site, as in our prior studies.[4,32-34] Those who reported first arrival at the site on the morning of 9/11 constituted the high exposure group as they were present during or immediately after the towers collapsed. The moderate exposure group included those who arrived in the afternoon of 9/11. The low exposure group included those who arrived between 9/12 and 9/24/2001. Non-FDNY firefighters from Chicago, Philadelphia, and San Francisco fire departments without WTC exposure were considered "non-WTC-exposed" and used as the reference group in firefighter analyses. Data from the NHIS were also used as a reference group for other comparisons.

CVD Risk Factors and Demographic Data

WTC-exposed and non-WTC exposed firefighters' demographic data, including sex, race, and birthdate were obtained from FDNY databases and fire department records from the other three cities. WTC-exposed firefighters complete a medical monitoring exam every 12 to 18 months that includes weight and height measurements for body mass index (BMI) and incorporates a self-administered, computer-based questionnaire, as previously described.[34] Non-WTC-exposed firefighters completed a similar questionnaire once, as described above. We obtained non-WTC-exposed firefighters' BMI from information provided on the questionnaire. All firefighters self-reported smoking status on their respective questionnaires as former, current, or never smokers. Former or current smokers were considered "ever smokers." CVD risk factors including hypertension, diabetes, and high cholesterol were self-reported on these health questionnaires; participants reported ever receiving a physician diagnosis of hypertension, diabetes, or high cholesterol.

Self-Reported Cardiovascular Disease (CVD)

The FDNY questionnaire is self-administered during the WTC-exposed participants' annual medical monitoring exam. A self-reported CVD diagnosis at the most recent questionnaire was based on a positive response to the question, "In the past 12 months, has a doctor or other health professional told you that you had any of the following? 1. Stroke/CVA or TIA; 2. Coronary artery disease, MI (heart attack), angina (ischemia) or blockage." The non-WTC-exposed firefighters included in this study each took a baseline questionnaire which includes questions about "ever" being diagnosed with CVD conditions. A self-reported CVD diagnosis was based on a positive response to the following question, "Has a doctor or other health professional ever told you that you had any of the following? 1. Stroke/CVA or TIA; 2. Coronary artery disease, MI (heart attack), angina (ischemia) or blockage." To obtain an appropriate "ever" comparison in the WTC-exposed cohort, we combined all prior FDNY questionnaire information from September 12, 2001 through May 26, 2021. For both cohorts, self-reported diagnoses were categorized as (1) self-reported stroke/TIA, (2) self-reported coronary artery disease, MI, angina, or blockage, henceforth referred to as "CAD", and (3) self-reported stroke or CAD which included reporting either or both of the two conditions, referred to as "stroke/CAD".

Validated Cardiovascular Disease

As self-reported CVD outcomes may be differentially reported based on different WTC exposure levels, we assessed agreement between self-reported CVD and confirmed cases only within the WTC-exposed

population through FDNY medical record review.[4] Medical record review was not available for the non-WTC-exposed firefighters.

National Health Interview Survey

We also compared firefighters to respondents of the 2019 NHIS cross-sectional interview survey of the US noninstitutionalized civilian population from all 50 states conducted by the National Center for Health Statistics.[35]

The 2019 version of the NHIS was chosen because the health questions were the most similar to the firefighter questionnaires. Data from NHIS participants were restricted to males aged 35+ years who did not reside in the South and answered CVD-related questions to be most comparable to the firefighter population and cities in this study, with a final sample population of 7,301 individuals. NHIS participants reported age in 2019, residence by region, race/ethnicity, height, weight, smoking status, and diagnoses of high cholesterol, diabetes, and hypertension. They also answered the questions, “Have you ever been told by a doctor or other health professional that you had: (1) a stroke?, (2) a heart attack, also called a myocardial infarction?, (3) angina, also called angina pectoris?, (4) coronary heart disease?” A positive answer to questions 2, 3, and 4 were classified as “CAD.” A positive answer to any of the above questions was classified as “stroke/CAD.” All diagnoses in this study are self-reported and henceforth will be referred to as stroke, CAD, and stroke/CAD. Individuals who reported stroke and reported CAD are included as events for both separate diagnoses, as well as for stroke/CAD.

Statistical analyses

Demographics and other characteristics were represented as proportions (%) and means (±SD) for the firefighter groups. Among all firefighters, multivariable logistic regression was used to estimate the association between WTC exposure (as both a binary variable, exposed vs non-exposed, and categorized, as above) and diagnoses of stroke, CAD, and stroke/CAD as binary variables (ever/never diagnosed). Two models were run to account for missing data. Model 1 only included variables that did not have any missing observations—age, race, and BMI. Model 2 additionally controlled for high cholesterol, diabetes, hypertension, and smoking status.

Within only the WTC-exposed group we evaluated the agreement between self-reported CVD and medical records. Positive predictive value (PPV) and sensitivity of self-reports were reported for all three CVD outcomes. Internal analyses were then conducted to assess associations between WTC exposure intensity and CVD outcomes within WTC-exposed firefighters only, with low exposure as the referent group, using multivariable logistic regression models included covariates in the same manner as described above. Two separate logistic models estimated the WTC exposure association with self-reported and with validated CVD outcomes.

Results

Demographic and other characteristics of the study population are displayed in Table 1. WTC-exposed firefighters were, on average, slightly younger on 9/11 (40 vs. 44), less likely to report ever smoking (33% vs. 44%), and more likely to be white (94% vs. 75%) than non-WTC-exposed firefighters. Over half of the WTC-exposed firefighters first arrived at the WTC site on the afternoon of 9/11/2001 (moderate exposure). A greater percentage of non-WTC-exposed firefighters reported a diagnosis of stroke/CAD than WTC-exposed firefighters. 47 (0.5%) WTC-exposed and 28 (1%) non-WTC-exposed firefighters reported having stroke and also reported having CAD. A greater proportion of non-WTC-exposed firefighters reported having diabetes or hypertension, while fewer reported having high cholesterol. WTC-exposed firefighters had 166 (2%) participants missing data for diabetes, hypertension, and high cholesterol and two participants missing data for smoking status. Non-WTC-exposed firefighters had 6 participants missing data for diabetes and 7 missing data for smoking status.

Odds of self-reported CAD were greater in highly (OR=1.48, 95% CI: 1.18, 1.86) and moderately (OR=1.31, 95% CI: 1.10, 1.57) exposed WTC firefighters compared with non-exposed firefighters after adjusting for age, race, and BMI (Table 2a). There was a significant trend for exposure, with greater exposure having a greater association with CAD (p for trend<0.0001). The same was not seen for stroke. Models which

additionally included CVD risk factors, also showed a significant exposure gradient for CAD and stroke/CAD, with greater exposure significantly associated with these outcomes (p for trend= 0.03 and 0.04, respectively, Table 2b).

When compared with the NHIS population, odds of all three CVD outcomes were significantly lower for both WTC-exposed and non-exposed firefighters when adjusting for age, race, and BMI (Table 3a). Models that additionally included CVD risk factors produced stronger protective estimates of CVD odds. Although all WTC-exposed firefighters had lower odds of all three CVD outcomes than the NHIS population, the magnitude of this protection was attenuated with increasing WTC exposure (p for trend <0.0001, Table 3b).

Medical record validation was only available for WTC-exposed FDNY firefighters. Agreement analyses restricted to WTC-exposed FDNY firefighters comparing self-reported CVD outcomes to medical record data showed a PPV of 56% and sensitivity of 79% for CAD and 37% PPV and 73% sensitivity for stroke. Multivariable logistic regression models within this firefighter population showed that the association between WTC exposure and all three medical record-validated CVD outcomes was attenuated compared to the association between exposure and self-reported CVD outcomes (Supplemental Tables 1a & 1b). However, a significant exposure gradient remained for both self-reported and validated outcomes for stroke/CAD.

Discussion

This study is the first to compare CVD outcomes in WTC-exposed firefighters to an occupationally similar non-WTC-exposed cohort. This comparison cohort allowed us to draw conclusions about the true association between WTC exposure and CVD outcomes while controlling for the potentially confounding variable of firefighter occupation. When adjusting for known risk factors, we observed a significant association of WTC exposure with CAD and stroke/CAD outcomes. Results were consistent with findings from prior studies of WTC-exposed populations, regardless of whether the respective outcomes were self-reported or clinically validated.[4,5,7,8] Compared with a general US population (NHIS), all firefighters had lower odds of all three CVD outcomes.

While the association between WTC exposure level and stroke alone was not statistically significant, there were significant associations of the exposure gradient with CAD and stroke/CAD outcomes. Prior work in FDNY firefighters found a similar exposure response for CVD confirmed with medical records.[4] Earlier arrival to the WTC disaster meant greater exposure to various toxicants that were present in the dust cloud.[1] As many of these substances are known cardiopulmonary hazards,[36] our results, even after controlling for the firefighting occupation, support prior studies demonstrating a significant association between WTC exposure and a greater risk of CVD.

Most prior work that has estimated the association between WTC exposure and CVD within FDNY rescue/recovery workers has been conducted solely through internal comparison. As CVD is a chronic disease, the necessity for an adequate comparison group is particularly evident more than 20 years after 9/11. Non-FDNY WTC-exposed cohorts have used the New York State, New York City, or US general populations as comparison groups.

However, firefighter activities may present an increased risk for CVD. For example, exposures during firefighting (response, fire suppression, and rescue work) have been shown to increase risk of sudden cardiac events five- to seven-fold compared with non-emergency activities.[11,37,38] This has been suggested to be largely due to activation and sustained arousal of the sympathetic nervous system, which can lead to increased cardiac stress.[28,39]

As such, US fire departments, including the four in this study, generally exclude individuals from hire or active duty that have been previously diagnosed with CAD, MI, angina, or stroke to ensure they will be able to perform essential job-tasks safely and effectively.[40] Our findings of a 28-49% reduction in any CVD odds in all firefighter groups compared with the general population is likely a result of the healthy worker effect. Prior work using data from the Career Firefighter Health Study investigating mortality through 2016 found mortality caused by heart/circulatory system diseases to be significantly lower for both WTC-exposed and non-exposed firefighters compared with the general population.[41] While the current study involves a subset of that source

population of firefighters, those alive in 2019, the overall findings highlight the health differences between firefighters and the general population. Fire department hiring practices combined with the retention of healthier individuals in the firefighting workforce highlights the importance of having a non-WTC-exposed firefighter comparison for WTC-related health studies.

There are limitations to this investigation. The use of self-reported outcomes is subject to measurement/recall bias. However, when compared with medical records, PPV and sensitivity for self-reported CVD in the WTC-exposed group are similar to published estimates in non-firefighting cohorts.[42-44] Additionally, it is possible that the WTC-exposed may overreport diagnoses compared with the non-WTC-exposed due to exposure and membership in the WTC Health Program, which provides no-cost annual medical monitoring and treatment for certified health conditions. However, our self-reported vs. medical record CVD agreement is higher than those in another WTC-exposed cohort (WTC Health Registry, which includes both 9/11 rescue/recovery workers and those who lived/worked in the vicinity).[45] Given that sensitivity proportions fall well within the published estimates, it is also likely that exposed and non-exposed firefighters may not be appreciably different from each other. Another limitation is that unmeasured confounding could have biased our results. For example, occupation data were not available for the 2019 NHIS. However, <1% of the US male population in 2019 were career firefighters.[46] Lastly, there could be differences in routine firefighting exposure or unique hiring considerations by city.

A strength of this study is that it is the first to account for the firefighting occupation when determining the association between WTC exposure and CVD. With respect to firefighters, we illustrated the need for an occupationally appropriate non-WTC-exposed comparison population when analyzing outcomes. Likely due to the healthy worker effect, the NHIS population may not be an adequate comparison population as it shows firefighting and WTC-exposure to be protective against CVD. Being able to account for the firefighting occupation provides improved comparison validity. This deserves consideration when studying other occupations where a healthy worker effect is expected.

Conclusion

The burden of disease was significantly greater in persons with a greater WTC exposure level, even though as a categorical variable, no WTC exposure level alone had statistically significantly greater CVD than the non-exposed firefighters when controlling for CVD risk factors. While the risk of CVD in WTC-exposed firefighters and non-WTC-exposed firefighters was significantly lower than that of a general US population (NHIS), we did observe a statistically significant exposure gradient where greater exposure was associated with a lower healthy worker protection from CVD. Adding to the current body of literature that has observed similar WTC exposure gradients for CVD is important for identifying those at risk. Future studies are needed to further explore this exposure-response gradient in firefighters, ideally with medical record documentation or other validated measures of CVD.

References

1. Lioy PJ, Weisel CP, Millette JR, et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. *Environ Health Perspect.* 2002;110(7):703-714.
2. An Z, Jin Y, Li J, Li W, Wu W. Impact of Particulate Air Pollution on Cardiovascular Health. *Curr Allergy Asthma Rep.* 2018;18(3):15.
3. Brook RD, Rajagopalan S, Pope CA, 3rd, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation.* 2010;121(21):2331-2378.
4. Cohen HW, Zeig-Owens R, Joe C, et al. Long-term Cardiovascular Disease Risk Among Firefighters After the World Trade Center Disaster. *JAMA Netw Open.* 2019;2(9):e199775.
5. Jordan HT, Miller-Archie SA, Cone JE, Morabia A, Stellman SD. Heart disease among adults exposed to the September 11, 2001 World Trade Center disaster: results from the World Trade Center Health Registry. *Prev Med.* 2011;53(6):370-376.

6. Remch M, Laskaris Z, Flory J, Mora-McLaughlin C, Morabia A. Post-Traumatic Stress Disorder and Cardiovascular Diseases: A Cohort Study of Men and Women Involved in Cleaning the Debris of the World Trade Center Complex. *Circ Cardiovasc Qual Outcomes.* 2018;11(7):e004572.
7. Sloan NL, Shapiro MZ, Sabra A, et al. Cardiovascular disease in the World Trade Center Health Program General Responder Cohort. *Am J Ind Med.* 2021;64(2):97-107.
8. Yu S, Alper HE, Nguyen AM, Maqsood J, Brackbill RM. Stroke hospitalizations, posttraumatic stress disorder, and 9/11-related dust exposure: Results from the World Trade Center Health Registry. *Am J Ind Med.* 2021;64(10):827-836.
9. Carter JM, Rayson MP, Wilkinson DM, Richmond V, Blacker S. Strategies to combat heat strain during and after firefighting. *Journal of Thermal Biology.* 2007;32(2):109-116.
10. de Lange AH, Kompier MA, Taris TW, et al. A hard day's night: a longitudinal study on the relationships among job demands and job control, sleep quality and fatigue. *J Sleep Res.* 2009;18(3):374-383.
11. Kales SN, Soteriades ES, Christophi CA, Christiani DC. Emergency duties and deaths from heart disease among firefighters in the United States. *N Engl J Med.* 2007;356(12):1207-1215.
12. Mittleman MA, Maclure M, Tofler GH, Sherwood JB, Goldberg RJ, Muller JE. Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. Determinants of Myocardial Infarction Onset Study Investigators. *N Engl J Med.* 1993;329(23):1677-1683.
13. Puttonen S, Harma M, Hublin C. Shift work and cardiovascular disease - pathways from circadian stress to morbidity. *Scand J Work Environ Health.* 2010;36(2):96-108.
14. Brandt-Rauf PW, Fallon LF, Jr., Tarantini T, Idema C, Andrews L. Health hazards of fire fighters: exposure assessment. *Br J Ind Med.* 1988;45(9):606-612.
15. Soteriades ES, Smith DL, Tsismenakis AJ, Baur DM, Kales SN. Cardiovascular disease in US firefighters: a systematic review. *Cardiol Rev.* 2011;19(4):202-215.
16. Choi B, Schnall P, Dobson M. Twenty-four-hour work shifts, increased job demands, and elevated blood pressure in professional firefighters. *Int Arch Occup Environ Health.* 2016;89(7):1111-1125.
17. Choi B, Steiss D, Garcia-Rivas J, et al. Comparison of body mass index with waist circumference and skinfold-based percent body fat in firefighters: adiposity classification and associations with cardiovascular disease risk factors. *Int Arch Occup Environ Health.* 2016;89(3):435-448.
18. Nor N, Lee CJ, Park KS, Chang S-J, Kim C, Park S. The risk of mortality and cardiovascular disease is increased in firefighters with elevated blood pressure compared to the general population. *Journal of Hypertension.* 2019;37:e11.
19. Smith DL, Haller JM, Korre M, et al. Pathoanatomic Findings Associated With Duty-Related Cardiac Death in US Firefighters: A Case-Control Study. *J Am Heart Assoc.* 2018;7(18):e009446.
20. Soteriades ES, Hauser R, Kawachi I, Liarokapis D, Christiani DC, Kales SN. Obesity and cardiovascular disease risk factors in firefighters: a prospective cohort study. *Obes Res.* 2005;13(10):1756-1763.
21. Martin ZT, Schlaff RA, Hemenway JK, et al. Cardiovascular Disease Risk Factors and Physical Fitness in Volunteer Firefighters. *Int J Exerc Sci.* 2019;12(2):764-776.
22. Smith DL, Fehling PC, Frisch A, Haller JM, Winke M, Dailey MW. The prevalence of cardiovascular disease risk factors and obesity in firefighters. *J Obes.* 2012;2012:908267.
23. Choi B, Dobson M, Schnall P, Garcia-Rivas J. 24-hour work shifts, sedentary work, and obesity in male firefighters. *Am J Ind Med.* 2016;59(6):486-500.
24. Haddock CK, Jitnarin N, Poston WS, Tuley B, Jahnke SA. Tobacco use among firefighters in the central United States. *Am J Ind Med.* 2011;54(9):697-706.
25. Jitnarin N, Poston WS, Haddock CK, Jahnke SA, Day RS. Tobacco use pattern among a national firefighter cohort. *Nicotine Tob Res.* 2015;17(1):66-73.
26. Noh J, Lee CJ, Hyun DS, et al. Blood pressure and the risk of major adverse cardiovascular events among firefighters. *J Hypertens.* 2020;38(5):850-857.
27. Fahy RF, Petrillo JT, Molis JL. *Firefighter Fatalities in the US - 2019.* NFPA Research: National Fire Protection Association;2020.
28. Smith DL, DeBlois JP, Kales SN, Horn GP. Cardiovascular Strain of Firefighting and the Risk of Sudden Cardiac Events. *Exerc Sport Sci Rev.* 2016;44(3):90-97.

29. Zeig-Owens R, Singh A, Triplett S, et al. Assembling the Career Firefighter Health Study cohort: A methods overview. *Am J Ind Med.* 2021;64(8):680-687.
30. Mueller AK, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. Comparing self-reported obstructive airway disease in firefighters with and without World Trade Center exposure. *Am J Ind Med.* 2023;66(3):243-251.
31. Daniels RD, Kubale TL, Yiin JH, et al. Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950-2009). *Occup Environ Med.* 2014;71(6):388-397.
32. Aldrich TK, Weakley J, Dhar S, et al. Bronchial Reactivity and Lung Function After World Trade Center Exposure. *Chest.* 2016;150(6):1333-1340.
33. Liu X, Yip J, Zeig-Owens R, et al. The Effect of World Trade Center Exposure on the Timing of Diagnoses of Obstructive Airway Disease, Chronic Rhinosinusitis, and Gastroesophageal Reflux Disease. *Front Public Health.* 2017;5:2.
34. Yip J, Webber MP, Zeig-Owens R, et al. FDNY and 9/11: Clinical services and health outcomes in World Trade Center-exposed firefighters and EMS workers from 2001 to 2016. *Am J Ind Med.* 2016;59(9):695-708.
35. National Center for Health Statistics. About the National Health Interview Survey. https://www.cdc.gov/nchs/nhis/about_nhis.htm. Accessed April 5, 2023.
36. Landrigan PJ, Lioy PJ, Thurston G, et al. Health and environmental consequences of the world trade center disaster. *Environ Health Perspect.* 2004;112(6):731-739.
37. Kales SN, Soteriades ES, Christoudias SG, Christiani DC. Firefighters and on-duty deaths from coronary heart disease: a case control study. *Environ Health.* 2003;2(1):14.
38. Smith DL, Haller JM, Korre M, et al. The Relation of Emergency Duties to Cardiac Death Among US Firefighters. *Am J Cardiol.* 2019;123(5):736-741.
39. Smith DL, Horn GP, Fernhall B, et al. Electrocardiographic Responses Following Live-Fire Firefighting Drills. *J Occup Environ Med.* 2019;61(12):1030-1035.
40. Technical Committee of Fire Service Occupational Safety and Health. *NFPA 1582: Standard on Comprehensive Occupational Medical Program for Fire Departments.* 2006.
41. Singh A, Zeig-Owens R, Cannon M, et al. All-cause and cause-specific mortality in a cohort of WTC-exposed and non-WTC-exposed firefighters. *Occup Environ Med.* 2023;80(6):297-303.
42. Haapanen N, Miilunpalo S, Pasanen M, Oja P, Vuori I. Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. *Am J Epidemiol.* 1997;145(8):762-769.
43. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol.* 2004;57(10):1096-1103.
44. Woodfield R, Group UKBSO, Follow-up UKB, Outcomes Working G, Sudlow CL. Accuracy of Patient Self-Report of Stroke: A Systematic Review from the UK Biobank Stroke Outcomes Group. *PLoS One.* 2015;10(9):e0137538.
45. Alper HE, Brite J, Cone JE, Brackbill RM. Comparison of prevalence and exposure-disease associations using self-report and hospitalization data among enrollees of the world trade center health registry. *BMC Med Res Methodol.* 2021;21(1):162.
46. Fahy R, Evarts B, Stein GP. *US Fire Department Profile 2019.* 2021.

Table 1: Demographic and Selected Characteristics of WTC-exposed and Non-WTC-exposed Firefighters

	WTC-exposed	Non-WTC-exposed	NHIS
n	9789	2729	7301
Stroke/CAD[1]	961 (9.8%)	319 (11.7%)	1053 (14.4%)
Stroke[2]	219 (2.2%)	91 (3.3%)	337 (4.6%)
CAD[3]	789 (8.1%)	256 (9.4%)	851 (11.7%)
Diabetes	1212 (12.4%)	516 (18.9%)	929 (12.7%)
Cholesterol	6372 (65.1%)	1539 (56.4%)	2613 (35.8%)
Hypertension	4470 (45.7%)	1375 (50.4%)	3140 (43.0%)

Mean BMI[4] (SD)	30.0 (4.6)	29.0 (4.4)	28.4 (4.6)
Mean Age on 9/11[5] (SD)	40.0 (7.4)	44.0 (8.8)	
Mean Age in 2019[5] (SD)	58.5 (7.4)	62.5 (8.8)	58.4 (14.0)
Ever smokers	3228 (33.0%)	1187 (43.5%)	3461 (47.4%)
Race			
White	9216 (94.1%)	2069 (75.8%)	5917 (81.1%)
Black	236 (2.4%)	298 (10.9%)	444 (6.1%)
Hispanic	308 (3.2%)	220 (8.1%)	419 (5.7%)
Other	29 (0.3%)	142 (5.2%)	521 (7.1%)
WTC Exposure			
High[6]	1597 (16.3%)		
Moderate[7]	5278 (53.9%)		
Low[8]	2957 (29.8%)		

Unless otherwise specified, all values in parentheses are percentages.
[1]Includes any report of stroke or CAD [2]Includes diagnoses of stroke/CVA or TIA
[3]Includes diagnoses of CAD, MI, or angina [4]in Kg/m^2 [5]in years [6]Arrived at the WTC site in the morning of 9/11/2001 [7]Arrived at the WTC site in the afternoon of 9/11/2001 [8]Arrived at the WTC site from 9/12-9/24/2001

Table 2a – Estimated odds ratios for self-reported CVD diagnoses by exposure status

	Stroke/CAD[1]		**Stroke[2]**		**CAD[3]**	
	OR (95% CI)		**OR (95% CI)**		**OR (95% CI)**	
	Model 1[4]	**Model 2[5]**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
WTC-exposed	1.23 (1.06, 1.43)	1.03 (0.88, 1.20)	1.03 (0.79, 1.35)	0.93 (0.71, 1.22)	1.25 (1.06, 1.47)	1.03 (0.87, 1.21)
Non-exposed	ref	ref	ref	ref	ref	ref

Table 2b – Estimated odds ratios for self-reported CVD diagnoses by exposure level

	Stroke/CAD[1]		**Stroke[2]**		**CAD[3]**	
	OR (95% CI)		**OR (95% CI)**		**OR (95% CI)**	
	Model 1[4]	**Model 2[5]**	**Model 1[4]**	**Model 2[5]**	**Model 1[4]**	**Model 2[5]**
High exposure	1.45 (1.18, 1.79)	1.19 (0.96, 1.48)	1.18 (0.80, 1.75)	1.04 (0.70, 1.55)	1.48 (1.18, 1.86)	1.20 (0.95, 1.51)
Moderate exposure	1.31 (1.11, 1.54)	1.10 (0.93, 1.30)	1.07 (0.79, 1.44)	0.97 (0.72, 1.30)	1.32 (1.10, 1.57)	1.09 (0.91, 1.31)
Low exposure	1.00 (0.83, 1.21)	0.83 (0.69, 1.01)	0.90 (0.64, 1.27)	0.81 (0.57, 1.15)	1.03 (0.84, 1.26)	0.85 (0.69, 1.05)
Non-exposed	ref	ref	ref	ref	ref	ref
P for trend	*P<0.0001*	*P=0.01*	*P=0.33*	*P=0.74*	*P<0.0001*	*P=0.03*

[1]Includes any report of stroke or CAD [2]Includes diagnoses of stroke/CVA or TIA [3]Inclused diagnoses of CAD, MI, or angina [4]Age, race, and BMI were also included in the model (complete case analysis, n=12,516) [5]Age, race, BMI, high cholesterol, diabetes, hypertension, smoking were also included in the model (complete case analysis, n=12,435)

Table 3a – Estimated odds ratios for self-reported CVD diagnoses in firefighters from all four cities compared with the NHIS population by exposure status

	Stroke/CAD[1]		Stroke[2]		CAD[3]	
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
	Model 1[4]	Model 2[5]	Model 1[4]	Model 2[5]	Model 1[4]	Model 2[5]
WTC-exposed	0.81 (0.73, 0.90)	0.62 (0.55, 0.70)	0.62 (0.51, 0.74)	0.54 (0.44, 0.66)	0.86 (0.77, 0.97)	0.64 (0.57, 0.73)
Non-exposed	0.71 (0.62, 0.82)	0.59 (0.51, 0.68)	0.66 (0.51, 0.84)	0.60 (0.47, 0.76)	0.74 (0.64, 0.87)	0.60 (0.51, 0.71)
NHIS Population	ref	ref	ref	ref	ref	ref

Table 3b – Estimated odds ratios for self-reported CVD diagnoses in WTC-exposed FDNY firefighters compared with the NHIS population by exposure level

	Stroke/CAD[1]		Stroke[2]		CAD[3]	
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
	Model 1[6]	Model 2[7]	Model 1[6]	Model 2[7]	Model 1[6]	Model 2[7]
High exposure	0.96 (0.80, 1.14)	0.71 (0.59, 0.86)	0.68 (0.48, 0.95)	0.58 (0.41, 0.82)	1.02 (0.84, 1.24)	0.74 (0.60, 0.91)
Moderate exposure	0.86 (0.76, 0.98)	0.66 (0.58, 0.76)	0.62 (0.49, 0.78)	0.55 (0.43, 0.69)	0.91 (0.79, 1.04)	0.68 (0.59, 0.79)
Low exposure	0.67 (0.58, 0.79)	0.51 (0.43, 0.60)	0.54 (0.40, 0.72)	0.47 (0.35, 0.63)	0.72 (0.61, 0.86)	0.53 (0.44, 0.63)
NHIS Population	ref	ref	ref	ref	ref	ref
P for trend	*P<0.0001*	*P<0.0001*	*P<0.0001*	*P<0.0001*	*P<0.0001*	*P<0.0001*

[1]Includes any report of stroke or CAD [2]Includes diagnoses of stroke/CVA or TIA [3]Inclused diagnoses of CAD, MI, or angina [4]Age, race, and BMI were included in the model (complete case analysis, n=19,354)
[5]Age, race, BMI, high cholesterol, diabetes, hypertension, smoking were included in the model (complete case analysis, n=19,099) [6]Age, race, and BMI were included in the model (complete case analysis, n=16,625) [7]Age, race, BMI, high cholesterol, diabetes, hypertension, smoking were included in the model (complete case analysis, n=16,377)

Publications

Journal Articles:

Mueller AK, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. PTSD symptoms, depressive symptoms, and subjective cognitive concerns in WTC-exposed and non-WTC-exposed firefighters. Am J Ind Med. 2021 Oct;64(10):803-814. doi: 10.1002/ajim.23285. Epub 2021 Aug 20. PMID: 34415073.

Webber MP, Singh A, Zeig-Owens R, Salako J, Skerker M, Hall CB, Goldfarb DG, Jaber N, Daniels RD, Prezant DJ. Cancer incidence in World Trade Center-exposed and non-exposed male firefighters, as compared with the US adult male population: 2001-2016. Occup Environ Med. 2021 Oct;78(10):707-714. doi: 10.1136/oemed-2021-107570. Epub 2021 Sep 10. PMID: 34507965; PMCID: PMC8458058.

Mueller AK, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. Comparing self-reported obstructive airway disease in firefighters with and without World Trade Center exposure. Am J Ind Med. 2023 Mar;66(3):243-251. doi: 10.1002/ajim.23455. Epub 2023 Jan 4. PMID: 36597815.

Singh A, Zeig-Owens R, Cannon M, Webber MP, Goldfarb DG, Daniels RD, Prezant DJ, Boffetta P, Hall CB. All-cause and cause-specific mortality in a cohort of WTC-exposed and non-WTC-exposed firefighters. Occup Environ Med. 2023 Jun;80(6):297-303. doi: 10.1136/oemed-2022-108703. Epub 2023 Mar 27. PMID: 36972975; PMCID: PMC10523283.

Mueller AK, Cohen H, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. Self-reported cardiovascular disease in career firefighters with and without World Trade Center exposure. J Occup Environ Med. 2023 Nov 1. doi: 10.1097/JOM.0000000000003007. Epub ahead of print. PMID: 37907410.

Conference Abstracts:

Singh A, Zeig-Owens R, Hall CB, Prezant DJ, Webber MP. Preliminary Cancer Findings from the Career Firefighter Health Study. North American Association of Central Cancer Registries Annual Meeting September 2020.

Mueller A, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. Self-reported obstructive airway disease in WTC-exposed firefighters compared with non-WTC-exposed firefighters. Oral Presentation. Society for Epidemiologic Research 2022 Annual Meeting Chicago June 15-17, 2022

Singh A, Zeig-Owens R, Cannon M, Webber David J. Prezant Paolo Boffetta Charles B. Hall. All-cause and cause-specific mortality in a cohort of WTC-exposed and non-WTC-exposed firefighters. Poster Presentation. Society for Epidemiologic Research 2022 Annual Meeting Chicago June 15-17, 2022

Singh A, Zeig-Owens R, Salako J, et al. The association between World Trade Center rescue/recovery work and obstructive sleep apnea in WTC-exposed and unexposed firefighters. Poster Presentation. Society for Epidemiologic Research 2022 Annual Meeting Chicago June 15-17, 2022

Mueller A, Zeig-Owens R, Singh A, Cohen HW, Webber MP, Prezant DJ. Comparing self-reported cardiovascular disease in career firefighters with and without World Trade Center Exposure. Poster Presentation. New York City Epidemiology Forum 2023.

Singh A, Zeig-Owens R, Webber MP, Mueller A, Prezant DJ. Self-reported chronic rhinosinusitis diagnoses and symptoms in WTC-exposed and non-WTC-exposed firefighters. Oral Presentation. New York City Epidemiology Forum 2023 New York June 5, 2023.

Inclusions

Cumulative Inclusion Enrollment Table

ACTUAL ENROLLMENT REPORT

Comments:

Racial Categories	Ethnic Categories									
	Not Hispanic or Latino			Hispanic or Latino			Unknown/ Not Reported Ethnicity			Total
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	8	50	0	0	0	0	0	0	0	58
Asian	54	467	0	0	0	0	0	0	0	521
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	205	3122	0	0	0	0	0	8	0	3335
White	633	29039	0	0	1	0	0	74	0	29747
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	73	0	93	1664	0	19	550	72	2471
Total	900	32751	0	93	1665	0	19	632	72	36132

Inclusion of gender and minority study subjects

There were no exclusions made on the bases of gender or minority status.

Inclusion of Children

No children were included in this study as all rescue/recovery workers were at least 18 years old on 9/11/2001.

Materials available for other investigators

Digital data are available for other investigators upon reasonable request and approval of all parties.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Zeig-Owens R, Singh A, Triplett S, Salako J, Skerker M, Napier A, Peele E, Stanley M, Sattaluri S, Prezant D, Webber MP. Assembling the Career Firefighter Health Study cohort: A methods overview. American journal of industrial medicine. 2021 August;64(8):680-687. PubMed PMID: 34114224; DOI: 10.1002/ajim.23266.
N/A: Not NIH Funded	Webber MP, Singh A, Zeig-Owens R, Salako J, Skerker M, Hall CB, Goldfarb DG, Jaber N, Daniels RD, Prezant DJ. Cancer incidence in World Trade Center-exposed and non-exposed male firefighters, as compared with the US adult male population: 2001-2016. Occupational and environmental medicine. 2021 October;78(10):707-714. PubMed PMID: 34507965; PubMed Central PMCID: PMC8458058; DOI: 10.1136/oemed-2021-107570.
N/A: Not NIH Funded	Mueller AK, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. Comparing self-reported obstructive airway disease in firefighters with and without World Trade Center exposure. American journal of industrial medicine. 2023 March;66(3):243-251. PubMed PMID: 36597815; DOI: 10.1002/ajim.23455.
N/A: Not NIH Funded	Mueller AK, Cohen H, Singh A, Webber MP, Hall CB, Prezant DJ, Zeig-Owens R. Self-reported cardiovascular disease in career firefighters with and without World Trade Center exposure. Journal of occupational and environmental medicine. 2023 November 1. PubMed PMID: 37907410; DOI: 10.1097/JOM.0000000000003007.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Category	Explanation
Other	https://careerfirefighterhealthstudy.org

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
170WEA	Y	Webber, Mayris P	MPH,MPH,DRPH,DRPH	PD/PI	2.4	0.0	0.0			NA
DPREZANT	N	PREZANT, DAVID J	MD,BS,MD,BA	Co-Investigator	1.0	0.0	0.0			NA
CHARLIEHALL21	N	Hall, Charles B	AB,MS,PHD,BA	Co-Investigator	1.0	0.0	0.0			NA
RZEIGOWENS	Y	Zeig-Owens, Rachel	DPH,MPH	Co-Investigator	2.0	0.0	0.0			NA
	N	Salako, Joke		Research Coordinator	4.2	0.0	0.0			NA
	N	Singh, Ankura	MPH	Biostatistician	2.3	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RS - Reentry Supplement
DS - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

File(s) uploaded:
Enrollment Report- Actual Updated.pdf

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

ACTUAL ENROLLMENT REPORT

Comments:

Racial Categories	Ethnic Categories									
	Not Hispanic or Latino			Hispanic or Latino			Unknown/ Not Reported Ethnicity			Total
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	8	50	0	0	0	0	0	0	0	58
Asian	54	467	0	0	0	0	0	0	0	521
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	205	3122	0	0	0	0	0	8	0	3335
White	633	29039	0	0	1	0	0	74	0	29747
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	73	0	93	1664	0	19	550	72	2471
Total	900	32751	0	93	1665	0	19	632	72	36132

Using Existing Dataset or Resource (Yes or No): Yes

Enrollment Location Type (Domestic or Foreign): Domestic

Enrollment Countries (List): USA

Enrollment Location:

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

The findings from this study provides insight into the WTC related conditions while controlling for the health worker effect and other occupational exposures.

Note: Uploaded attachment in Section B.2 as recommended in CDC closeout requirements.