Mortality Among World Trade Center Rescue and Recovery Workers, 2002–2011

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Background *Rescue and recovery workers responding to the 2001 collapse of the World Trade Center (WTC) sustained exposures to toxic chemicals and have elevated rates of multiple morbidities.*

Methods *Using data from the World Trade Center Health Program and the National Death Index for 2002–2011, we examined standardized mortality ratios (SMR) and proportional cancer mortality ratios (PCMR) with indirect standardization for age, sex, race, and calendar year to the U.S. general population, as well as associations between WTC-related environmental exposures and all-cause mortality.*

Results *We identified 330 deaths among 28,918 responders (SMR 0.43, 95%CI 0.39–0.48). No cause-specific SMRs were meaningfully elevated. PCMRs were elevated for neoplasms of lymphatic and hematopoietic tissue (PCMR 1.76, 95%CI 1.06–2.75). Mortality hazard ratios showed no linear trend with exposure.*

Conclusions *Consistent with a healthy worker effect, all-cause mortality among responders was not elevated. There was no clear association between intensity and duration of exposure and mortality. Surveillance is needed to monitor the proportionally higher cancer mortality attributed to lymphatic/hematopoietic neoplasms.* Am. J. Ind. Med. © 2015 Wiley Periodicals, Inc.

KEY WORDS: World Trade Center attack, 2001; mortality; occupational exposure; epidemiology; cohort study

INTRODUCTION

Rescue and recovery workers responding to the September 11, 2001 World Trade Center (WTC) collapse sustained unprecedented exposures to a complex mix of toxic chemicals [Lioy et al., 2002; Lioy and Georgopoulos 2006]. Analysis of settled dust and smoke collected in the week after the disaster identified metals, radionuclides, ionic species, asbestos, inorganic species, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, polychlorinated dibenzodioxins, polychlorinated dibenzofurans, pesticides, phthalate esters, brominated diphenyl ethers, and other hydrocarbons [Lioy et al., 2002; Offenberg et al., 2004]. The dust and smoke samples were primarily comprised of construction materials, soot, leaded and unleaded paint, and glass fibers [Lioy et al., 2002]. Rescue and recovery workers

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and volunteers (responders) exhibit persistent rates of multiple morbidities, including asthma, sinusitis, gastroesophageal reflux disease, spirometric abnormalities, and mental health disorders (depression, post-traumatic stress disorder, panic disorder) [Wisnivesky et al., 2011]. Increases in self-reported heart disease [Jordan et al., 2011b] and hospitalizations for cardiovascular and cerebrovascular diseases [Jordan et al., 2013] have been observed among community survivors. A modest excess of some neoplasms has also been reported among community survivors [Li et al., 2012], responders [Solan et al., 2013], and firefighters [Zeig-Owens et al., 2011], although associations between intensity of exposure and cancer were inconsistent.

A single study examined mortality from 2003 to 2009 among a mixed group of WTC community survivors (n = 28,593) and responders (n = 13,337) participating in the New York City Department of Health and Mental Hygiene's (DOHMH) WTC Health Registry [Jordan et al., 2011a]. Age, sex, race, and calendar year adjusted standardized mortality ratios (SMR) were lower than expected for all causes of death. Among community survivors, greater as compared to lesser exposure was significantly associated with all-cause and heart disease-related mortality.

The WTC Health Program (WTCHP) provides medical monitoring and treatment for general responders who worked or volunteered onsite in rescue, recovery, demolition, debris cleanup, or related support services [Herbert et al., 2006; Moline et al., 2008]. Over 30,000 men and women were seen at the WTCHP at least once between the start of the program in July 2002 and December 2011. With matching data from the National Death Index (NDI) for the period 2002–2011, we examined SMR, proportional mortality ratios (PMR), proportional cancer mortality ratios (PCMR), and the association between WTC-related environmental exposures and all-cause mortality in this cohort of responders.

MATERIALS AND METHODS

Study Population

The WTCHP has been described in detail elsewhere [Herbert et al., 2006; Moline et al., 2008; Dasaro et al., 2015]. In brief, 30,947 responders enrolled in the program between July 16, 2002 and December 31, 2011 and completed examinations that included demographic, medical, mental health, and exposure assessment questionnaires; physical examinations; spirometry; and chest X-rays. Enrollment in the WTCHP has been continuous since 2002. The present analyses include program members from all clinical sites (Icahn School of Medicine at Mount Sinai; New York University School of Medicine; North Shore-LIJ Health System; State University of New York, Stony Brook; Rutgers University) who enrolled by the end of 2011 and consented to participate in research (n = 28,918). The study was approved by the Mount Sinai Program for the Protection of Human Subjects.

Exposure Assessment

WTC-related environmental exposure was derived from self-reported exposure assessment questionnaires. Exposure was categorized into four mutually exclusive groups to reflect the intensity and duration of exposure to the dust, smoke, and debris: very high, high, intermediate, and low [Wisnivesky et al., 2011]. Group assignment was based on the total time spent working at the WTC site, exposure to the cloud of debris from the collapse of the buildings, and work on the pile of debris [Wisnivesky et al., 2011]. Very high exposure encompasses those who worked more than 90 days, were exposed to the dust cloud, and worked on the pile. High exposure consists of those who were exposed to the dust cloud, but either worked less than 90 days or did not work on the pile. Intermediate exposure consists of those not exposed to the dust cloud and either worked between 40 and 90 days or worked on the pile. Low exposure consists of those who worked less than 40 days, were not exposed to the dust cloud, and did not work on the pile. This four-level exposure metric was associated with incidence of chronic disease [Wisnivesky et al., 2011] and cancer [Solan et al., 2013].

As an alternative exposure metric, we used a set of three variables separately detailing dust cloud exposure, including arrival time, duration of work (quartiles), and location of work (on the debris pile, not on the debris pile) [Solan et al., 2013]. Dust cloud exposure was categorized for responders who reported being south of Canal Street on 9/11 by whether they were engulfed in the dust cloud, exposed to significant amounts of dust but not engulfed in the cloud, exposed to some dust, or not exposed to dust [Solan et al., 2013]. Responders not exposed to the dust cloud were further categorized by early (9/11–9/14/2001) or late (9/15/2001 or later) arrival at the WTC site.

Mortality Assessment

NDI is a centralized database of death records from state-based vital statistics offices [National Center for Health Statistics, 2013a]. We provided NDI with identifying information (first/last names, date of birth, sex, race, marital status, social security number [SSN], state of residence) for 12,741 workers in two batches: 2,725 unique records in 2008, 5,209 unique records in 2011, and 4,807 records included in both in 2008 and 2011. SSN was available for 4,746 of the records (37%). For the majority (88%) of this group SSN was available from the enrollment questionnaire, which

requested SSN from 2002 to 2005. For the remaining participants, SSN was collected when they received care at the Mount Sinai site for WTCHP-covered conditions. We used NDI recommended scores for probabilistic matching [National Center for Health Statistics, 2013a] to identify deaths among responders through December 31, 2011. Underlying cause of death was available as International Classification of Disease 10th Revision (ICD-10) codes [World Health Organization, 2004]. Information on responders with WTCHP follow-up visits after 2011 (n = 16,177) was not sent to NDI because they were known to be alive at the end of the study period.

Statistical Analysis

First, we calculated SMRs and 95% confidence intervals (CI) [Sahai and Khurshid, 1993] with indirect standardization for age (5-year groups), sex, race (white, not white), and calendar year from 2002 to 2011 to compare all-cause and cause-specific mortality among responders to mortality in the U.S. general population [CDC, 2013]. The U.S. general population was selected as the referent because responders resided in several states. For each responder, yearly expected mortality was summed over the years at risk for that individual.

Second, to examine whether the proportional distribution of causes of death differed between responders and the U.S. general population [CDC, 2013] regardless of whether overall mortality was elevated we calculated PMRs and 95%CIs [Breslow and Day, 1987] with indirect standardization for age (5-year groups), sex, race (white, non-white), and calendar year from 2002 to 2011. For cancer deaths we also calculated PCMRs and 95%CIs [National Center for Health Statistics, 2013b] with indirect standardization for age (5-year groups), sex, race (white, non-white), and calendar year from 2002 to 2011. PCMRs use cancer deaths—as opposed to all deaths—as the denominator. Causes of death were mapped to the National Institute for Occupational Safety and Health (NIOSH) major cause of death categories [Robinson et al., 2006].

Third, to examine the association between WTC-related environmental exposure and mortality we used multivariable Cox regression. Survival time began accruing at study enrollment and ended at the earlier time of death, December 31, 2008 (for responders whose records were sent to NDI in 2008 only and did not return for a WTCHP visit), or December 31, 2011. We ran unadjusted and adjusted models. The adjusted model included age (linear and quadratic) on 9/11/2001; occupation pre-9/11/2001 (protective services, construction, other); sex; race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other); year of WTCHP enrollment (2001–2005, 2006–2008, 2009–2011); smoking at enrollment (never, former, current);

TABLE I. Characteristics of World Trade Center Health Program Rescue and Recovery Worker Participants, 2002–2011 (n = 28,918)

Characteristic	N	Percent	Deaths (N)
Person-years of observation	164,563		330
Age on 9/11/2001, years (mean ± SD)	38.8 ± 8.8		330
Sex			
Male	24,632	85.2	299
Female	4,286	14.8	31
Race/ethnicity			
Non-hispanic white	18,317	63.3	229
Non-hispanic black	3,065	10.6	39
Hispanic	6,171	21.3	49
Other	1,365	4.7	13
Exposure index			
Low	4,041	14.7	45
Intermediate	17,728	64.3	212
High	4,908	17.8	56
Very high	903	3.3	9
Dust cloud exposure/arrival time			
No dust/late arrival (9/15 and later)	6,530	23.5	93
No dust/early arrival (9/11–9/14)	8,479	30.5	103
Some exposure to dust cloud	2,069	7.4	17
Significant exposure to dust cloud	4,845	17.4	43
Directly in dust cloud	5,870	21.1	65
Duration of work (days)			
1–16	6,857	24.3	76
17–51	6,884	24.4	78
52–111	7,111	25.2	72
≥112	7,360	26.1	98
Location of work			
Not on debris pile	17,749	63.4	205
On debris pile	10,253	36.6	119
Occupation pre-9/11/2001			
Protective services	13,676	47.3	64
Construction	6,283	21.7	125
Other	8,959	31.0	141
Year of program enrollment			
2002–2005	13,543	46.8	237
2006–2008	9,689	33.5	76
2009–2011	5,686	19.7	17
Smoking at program enrollment			
Never	17,118	60.1	140
Former	6,974	24.5	96
Current	4,413	15.5	89
BMI at program enrollment			
Normal	4,417	15.8	67
Overweight	12,025	42.9	116
Obese	11,587	41.3	130
SSN submitted to NDI			
No	18,997	65.7	152
Yes	9,921	34.3	178

SD, standard deviation; BMI, body mass index; SSN, social security number; NDI, national death index.

TABLE II. Observed Deaths and Standardized Mortality Ratios* for World Trade Center Health Program Rescue and Recovery Worker Participants, 2002–2011 (n = 28,918)

Year	Deaths (N)	SMR	95%CI
2002	1	0.42	0.01–2.35
2003	7	0.29	0.12–0.60
2004	12	0.28	0.15–0.50
2005	25	0.49	0.32–0.73
2006	37	0.60	0.42–0.82
2007	45	0.54	0.39–0.72
2008	43	0.42	0.30–0.57
2009	40	0.35	0.25–0.48
2010	50	0.38	0.28–0.50
2011	70	0.46	0.36–0.58
Total	330	0.43	0.39–0.48

SMR, standardized mortality ratio; CI, confidence interval.
*Indirect standardization for age, sex, calendar year to U.S. general population mortality rates.

and measured body mass index (BMI; normal, overweight, obese) at enrollment [World Health Organization, 2015]. "Other" pre-9/11/2001 occupation was primarily comprised of installation, maintenance, and repair workers and transportation and material moving workers.

Fourth, the WTCHP received unsolicited reports of deaths from next-of-kin. The WTCHP makes no systematic effort nor conducts outreach to identify deaths among responders; death notifications from next-of-kin are spontaneous and voluntary. Date of death was not collected from next-of-kin so we made the assumption that deaths reported by July 2012 had occurred within our study period. We used capture recapture methods stratified by year of enrollment (2001–2005, 2006–2008, 2009–2011) to estimate the total number of identified and unidentified deaths among responders [Wittes et al., 1974].

Lastly, to determine the robustness of our results to model misspecification and outcome misclassification we performed several secondary analyses: (i) occupation pre-9/11/2001 was directly related to a responder's functional role in the rescue and recovery efforts and a responder's role on site was related to intensity and duration of exposure. To address the possibility of over-adjustment we ran a model without occupation; (ii) BMI at enrollment was missing for 889 responders, including 17 deceased responders. To maximize the number of included deaths we ran a model without BMI; (iii) To explore whether lack of SSN, which likely limited identification of deaths through NDI, may have biased the association between exposure and mortality we ran the Cox models additionally adjusting for availability of SSN; (iv) we ran a logistic regression model including the next-of-kin reported deaths. All statistical analyses were performed in SAS version 9.4 (Cary, NC).

RESULTS

The mean (standard deviation) age of the responders on September 11, 2001 was 38.8 (8.8) years (Table I). The majority of responders was male (85%), non-Hispanic white (63%), and at the time of enrollment in the WTCHP had never smoked (60%). Almost half (47%) of responders enrolled in the WTCHP from 2002 to 2005. Most responders (64%) were categorized as having intermediate level exposure to dust, smoke, and debris from the WTC site. With NDI matching we identified 330 deaths among responders through the end of 2011; cause of death was available for 329 of the deaths.

The SMR standardized for age, sex, race, and calendar year for the period 2002–2011 was 0.43 (95%CI 0.39–0.48; Table II). SMRs have not been increasing significantly over time ($P = 0.90$). None of the cause-specific SMRs were meaningfully elevated (Table III).

Among the 329 deceased responders with NDI data on major cause of death, PMRs standardized for age, sex, race, and calendar year showed a higher than expected proportion of deaths due to malignant neoplasms of digestive organs and the peritoneum (PMR 1.74, 95%CI 1.26–2.35) and neoplasms of lymphatic and hematopoietic tissue (PMR 2.49, 95%CI 1.50–3.89; Table III). When examining the proportional distribution of causes of death among just cancer deaths only neoplasms of lymphatic and hematopoietic tissue (PCMR 1.76, 95%CI 1.06–2.75; Table III) remained statistically elevated. Lower than expected proportions of deaths were observed for other diseases of the circulatory system (PMR 0.44, 95%CI 0.19–0.87) and diseases of the digestive system (PMR 0.46, 95%CI 0.21–0.86).

In the Cox regression for all-cause mortality, confidence limits for the exposure effect estimate were wide and encompassed the null value. In unadjusted models with the four-level exposure metric, responders exposed to very high as compared to low WTC-related environmental exposures had hazard ratios (HR) below 1.0 (Table IV; HR 0.79, 95% CI 0.38–1.61). In adjusted models, responders exposed to very high as compared to low WTC-related environmental exposures had HR above 1.0 (HR 1.22, 95%CI 0.57–2.63), adjusted for age on 9/11/2001, occupation pre-9/11/2001, sex, race/ethnicity, year of enrollment, and smoking and BMI at enrollment. There was no linear trend with exposure for either unadjusted ($P = 0.57$) or adjusted ($P = 0.25$) models. Results were comparable for the models using the alternative exposure metric incorporating separate measures for dust cloud exposure, duration on site, and location of work (Table IV).

TABLE III. Number of Observed Deaths, Cause-specific Standardized Mortality Ratios,* Proportional Mortality Ratios,* and Proportional Cancer Mortality Ratios* for World Trade Center Health Program Rescue and Recovery Worker Participants, 2002–2011 (n = 329)

Major cause of death (NIOSH number)	Deaths	SMR	95%CI	PMR	95%CI	PCMR	95%CI
Tuberculosis and HIV related disease (01)	5	0.30	0.10–0.70	0.77	0.25–1.80		
Malignant neoplasm of buccal cavity and pharynx (02)	2	0.41	0.05–1.48	0.94	0.11–3.38	0.65	0.08–2.34
Malignant neoplasm of digestive organs and peritoneum (03)	42	0.76	0.55–1.03	1.74	1.26–2.35	1.21	0.87–1.64
Malignant neoplasm of respiratory system (04)	28	0.48	0.32–0.69	1.08	0.72–1.56	0.75	0.50–1.08
Malignant neoplasm of breast (05)	2	0.36	0.04–1.32	0.83	0.10–2.99	0.61	0.07–2.19
Malignant neoplasm of female genital organs (06)	2	0.65	0.08–2.37	1.50	0.18–5.39	1.11	0.13–4.00
Malignant neoplasm of male genital organs (07)	1	0.15	0.00–0.86	0.35	0.01–1.92	0.25	0.01–1.41
Malignant neoplasm of urinary organs (08)	5	0.54	0.17–1.25	1.18	0.38–2.76	0.81	0.26–1.90
Malignant neoplasm of other and unspecified sites (09)	20	0.63	0.39–0.98	1.43	0.88–2.21	1.01	0.62–1.56
Neoplasms of lymphatic and hematopoietic tissue (10)	19	1.09	0.66–1.70	2.49	1.50–3.89	1.76	1.06–2.75
Benign and unspecified neoplasms (11)	3	1.15	0.24–3.36	2.64	0.54–7.69		
Diseases of the blood and blood forming organs (12)	0	0	0.00–1.32	0	0.00–3.05		
Diabetes mellitus (13)	8	0.33	0.14–0.64	0.76	0.33–1.50		
Mental, psychoneurotic, and personality disorders (14)	7	0.48	0.19–1.00	1.13	0.45–2.33		
Disorders of the nervous system and sense organs (15)	3	0.18	0.04–0.53	0.41	0.08–1.20		
Diseases of the heart (16)	59	0.35	0.27–0.46	0.81	0.62–1.05		
Other diseases of the circulatory system (17)	8	0.19	0.08–0.37	0.44	0.19–0.87		
Diseases of the respiratory system (18)	18	0.46	0.27–0.72	1.02	0.60–1.61		
Diseases of the digestive system (19)	9	0.20	0.09–0.37	0.46	0.21–0.86		
Diseases of the skin and subcutaneous tissue (20)	0	0	0.00–3.68	0	0.00–8.58		
Disease of the musculoskeletal system and connective system (21)	2	0.69	0.08–2.49	1.6	0.19–5.78		
Diseases of the genitourinary system (22)	4	0.35	0.09–0.89	0.81	0.22–2.08		
Symptoms and ill-defined conditions (23)	6	0.53	0.19–1.14	1.27	0.46–2.76		
Transportation injuries (24)	15	0.43	0.24–0.71	1.07	0.60–1.77		
Falls (25)	4	0.68	0.18–1.73	1.57	0.43–4.02		
Other injury (26)	20	0.39	0.24–0.60	0.96	0.59–1.48		
Violence (27)	23	0.46	0.29–0.70	1.15	0.73–1.73		
Other causes (residuals and blank codes; 28)	14	0.41	0.23–0.70	0.97	0.53–1.62		

NIOSH, national institute for occupational safety and health; SMR, standardized mortality ratio; CI, confidence interval; PMR, proportional mortality ratio; PCMR, proportional cancer mortality ratio.

*Indirect standardization for age, sex, race, calendar year to U.S. general population mortality rates.

The WTCHP received 305 unsolicited reports from next-of-kin for responder deaths. Two hundred and fifty of these reports corroborated deaths we had identified through NDI matching, but 55 of these reports were newly identified deaths. The only statistically significant difference in socio-demographic or exposure characteristics between the 55 persons identified through next-of-kin report only and the 330 deaths identified through NDI were year of enrollment and availability of SSN. SSN was available for 54% of the NDI identified deaths as compared to 33% of the next-of-kin identified deaths ($P < 0.01$). With year-of-enrollment-stratified capture-recapture analysis we estimated total mortality among responders to be 402, which included 330 deaths identified through NDI, 55 deaths identified through next-of-kin, and 17 expected deaths that were not identified through either method.

There were no substantively meaningful changes to the association between WTC-related exposure and mortality in secondary analyses when we removed occupation or BMI from the model, or included the 55 deaths reported by next of kin (data not shown). Adjusting for availability of SSN did not substantively change the association between WTC-related exposure and mortality (data not shown).

DISCUSSION

In the 10 years following the WTC disaster, all-cause and cause-specific mortality in this cohort of responders was less than expected in comparison to the U.S. general population. Using multiple measures of the intensity and duration of environmental exposures experienced at the site, there appeared to be no clear association between exposure and mortality through the end of 2011. In adjusted models the HRs were elevated for high and very high

TABLE IV. Unadjusted and Adjusted* Hazard Ratios for Association Between World Trade Center-Related Environmental Exposure and All-Cause Mortality Among World Trade Center Health Program Rescue and Recovery Worker Participants, 2002–2011 (n = 26,634)

	Unadjusted (n = 322 deaths)		Adjusted* (n = 304 deaths)	
Exposure metric	**HR**	**95%CI**	**HR**	**95%CI**
Model with 1-variable exposure metric				
Exposure index				
Low	1.00		1.00	
Intermediate	0.95	0.69–1.31	1.09	0.77–1.52
High	0.94	0.63–1.38	1.27	0.84–1.90
Very High	0.79	0.38–1.61	1.22	0.57–2.63
		p-trend = 0.57		p-trend = 0.25
Model with 3-variable exposure metric				
Dust cloud exposure/arrival time				
No dust/late arrival (9/15 or later)	1.00		1.00	
No dust/early arrival (9/11–9/14)	0.91	0.69–1.22	1.04	0.77–1.40
Some exposure to dust cloud	0.65	0.39–1.09	0.85	0.49–1.47
Significant exposure to dust cloud	0.65	0.45–0.94	0.85	0.58–1.24
Directly in dust cloud	0.81	0.59–1.12	1.13	0.81–1.59
		p-trend = 0.05		p-trend = 0.88
Duration of work (days)				
1–16	1.00		1.00	
17–51	1.03	0.75–1.41	1.24	0.89–1.73
52–111	0.86	0.62–1.19	1.08	0.77–1.52
≥112	1.05	0.77–1.42	1.07	0.78–1.48
		p-trend = 0.99		p-trend = 0.86
Location of work				
Not on debris pile	1.00		1.00	
On debris pile	1.04	0.82–1.31	1.09	0.85–1.39

HR, hazard ratio; CI, confidence interval; BMI, body mass index.
*Adjusted for age on 9/11/2001, occupation pre-9/11/2001, sex, race/ethnicity, year of enrollment, and smoking and BMI at enrollment.

as compared to low exposure, but the estimates were imprecise, broadly encompassed the null, and there was no monotonic trend between increasing exposure and death. Among deaths to cancer, however, there were proportionally more to neoplasms of lymphatic and hematopoietic tissue as compared to the U.S. general population.

The reduced mortality among responders supports the findings of Jordan et al. [2011b] for rescue and recovery workers enrolled in the New York City DOHMH WTC Health Registry. The SMR we observed for the period 2002–2011 (0.43, 95%CI 0.39–0.48) was remarkably similar to the DOHMH's SMR for the period 2002–2009 (0.45, 95% CI 0.38–0.53). Additionally, our study and the DOHMH study both reported no meaningful association between WTC-related environmental exposure and all-cause mortality. Approximately 20% of responders enrolled in the WTCHP are included in the DOHMH WTC Health Registry [Solan et al., 2013].

Lower mortality among responders as compared to the general population is not surprising. Not only were these men and women healthy enough to participate in the rescue and recovery operations in 2001, but many were employed in physically demanding occupational sectors, such as construction, or were members of the New York City Police Department (NYPD), which requires a pre-employment physical fitness test. We would expect mortality among our cohort of responders to be lower than similarly aged people in the general population, which is known as the healthy worker effect. Working populations generally experience mortality rates about 15% below the general population [Meijers et al., 1989] and active workers in safe environments are estimated to have mortality rates 60–90% below the general population [McMichael, 1976]. The approximately 55% reduction in all-cause mortality in our cohort is indicative of the exceptional health status of responders at baseline. This phenomenon, termed the healthy hire effect, is reflective of healthy individuals being more likely than unhealthy individuals to seek and gain employment [Arrighi

and Hertz-Picciotto, 1994]. A related bias, the healthy worker survivor effect, describes the situation where those who remain employed tend to be healthier than those who left the workforce [Arrighi and Hertz-Picciotto, 1994]. The healthy worker survivor effect is a common concern in many occupational cohorts because the bias could mask weak effects between exposure and mortality. The healthy worker survivor effect, however, is not applicable to our examination of WTC-related environmental exposure and mortality because cleanup at the WTC site was completed in May 2002. Responders remaining healthy and in the work force in the intervening years were not accruing additional WTC-related exposures, although they could have ongoing relevant occupational exposures through other employment.

Another explanation for the reduced mortality rates among responders despite exposure to toxic chemicals is their participation in the WTCHP. The monitoring (beginning July 2004) and treatment (beginning October 2006) received through the program may identify disease earlier and increase survival as compared to the general population. The continuous nature of enrollment into the WTCHP may also introduce bias. Over half the cohort enrolled since 2006. Responders only contribute person-time to the analyses once enrolled so in this study late enrollees contributed less time at risk of death as compared to early enrollees. Late enrollees had to be healthy enough to survive until enrollment, but regardless of whether they die soon after enrollment or remain healthy through the end of the study period the timing of their entry into the cohort may bias the overall SMR.

This relation between year of enrollment and death is further complicated by availability of SSN; less than 40% of our population had SSN on file. SSN was collected at enrollment only through 2005 so responders with SSN may contribute more person-time to the analysis, and if deceased may be more reliably identified through NDI. It does not appear, though, that availability of SSN substantially impacted our results. A proportional hazards model with a term for SSN submitted to NDI did not meaningfully change the HRs for the exposure effect. Additionally, using year-stratified capture-recapture analyses to compare deaths identified through NDI to deaths identified through unsolicited next-of-kin report, we estimated a net under counting of just 72 deaths from NDI matching.

PMRs can be challenging to interpret. Within a group, PMRs relate cause-specific to all-cause mortality and approximate the ratio of the cause-specific SMR to the all-cause SMR. SMRs are notably confounded in occupational cohorts because of a lack of suitable comparison population; PMRs appear somewhat less susceptible to this lack of comparability [Park et al., 1991], especially for non-malignant conditions [Wong et al., 1985]. PMRs may help identify whether there is an increased frequency of disease among a particular group [Roman et al., 1984], but a PMR for one condition may be distorted by the rates of another condition [Kupper et al., 1978]. Additionally, PMRs may be falsely elevated when a group's all-cause SMR is below one [Roman et al., 1984]. In this population there are two significantly low PMRs and the SMR is below one, both factors that may have artificially inflated PMRs.

The elevated PMRs for malignant neoplasms of digestive organs and the peritoneum and neoplasms of lymphatic and hematopoietic tissue indicate that among all deaths proportionally more than expected were attributed to these two major causes. PMRs using the general population as the comparison group, however, tend to overstate risk and are impacted more by the healthy worker effect than PCMRs, which are based just on cancer deaths [Wong et al., 1985]. Cancer is less susceptible to the healthy worker effect than, for example, cardiovascular disease [Wong et al., 1985]. Although PCMRs appear to estimate risk of cancer death better than PMRs, even PCMRs may poorly estimate the true magnitude of risk [Wong et al., 1985]. When we used PCMRs to focus specifically on cancer deaths, only deaths to neoplasms of lymphatic and hematopoietic tissue remained statistically elevated.

In previous analyses of the WTCHP responder cohort there was no overall increased incidence of lymphatic/hematopoietic cancers through 2008 [Solan et al., 2013], although a study of responders in the New York City DOHMH WTC Health Registry reported an elevated incidence of multiple myeloma from 2007 to 2008 [Li et al., 2012]. The biological plausibility of these cancers resulting from WTC exposure is uncertain. Chemical exposure is a risk factor for some lymphatic/hematopoietic cancers [Hosnijeh et al., 2012]. Additionally, lymphatic/hematopoietic cancers are thought to have shorter latencies than solid tumors [Armenian and Lilienfeld, 1974], which may be meaningful within 10 years of follow-up.

Expected associations for well-established risk factors for premature mortality provide confidence in the quality of our data. For instance, in the adjusted models, current smokers were more likely to have died as compared to never smokers and responders who were overweight as compared to normal weight at program enrollment had a moderate decrease in risk of death [Flegal et al., 2013]. The apparent confounding between the unadjusted and adjusted Cox regression models may indicate that at this time typical risk factors, such as age, sex, and smoking history are more strongly related to risk of death than WTC-related environmental exposures.

Also noteworthy was an association between occupation pre-9/11/2001 and mortality. In adjusted analyses, mortality among construction and other workers was elevated in comparison to protective services, which was comprised primarily of NYPD. This finding corroborates previous research showing decreased prevalence of self-reported WTC-related health problems among NYPD as compared to

non-NYPD responders [Perrin et al., 2007; Wisnivesky et al., 2011].

Enrollment in the WTCHP is voluntary. Self-selection into the program may decrease the generalizability of results to the broader population of responders. Additionally, although our study cohort of nearly 30,000 is well-defined, there is no count of the total number of persons involved in WTC-related rescue, recovery, and clean-up operations. The number of rescue and recovery workers and volunteers is estimated at 60,000–70,000 [Savitz et al., 2008] to over 90,000 [Murphy et al., 2007]. Our reliance on self-reported exposure is also a limitation.

With 10 years of follow-up after the WTC attacks, all-cause and cause-specific mortality ratios among rescue and recovery workers and volunteers enrolled in the WTCHP are not elevated, and there does not appear to be an association between intensity and duration of WTC-related environmental exposure and mortality. There are suggestive indications of a proportional elevation among cancer deaths due to neoplasms of lymphatic and hematopoietic tissues, but additional study and time are needed to better understand these findings. In general, lower mortality in a cohort of workers healthy at baseline is expected. It is uncertain, though, whether the low mortality observed through 2011 will endure into the future. It is possible that the 10 year follow-up period is too short to observe WTC-related mortality, particularly for a relatively young population. The generally lower mortality rates among responders through 2011 may not persist into the future if WTC-related mortality were to emerge as a result of diseases with long latencies or long median survival times. Only with continued monitoring can we fully appreciate the long-term ramifications of the toxic exposures from the rescue, recovery, and cleanup operations at the WTC.

AUTHOR'S CONTRIBUTIONS

All authors made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and drafted the work or revised it critically for important intellectual content; and provided final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ETHICS REVIEW AND APPROVAL

This study was approved by the Mount Sinai Program for the Protection of Human Subjects. Participants signed written informed consent.

DISCLOSURE BY AJIM EDITOR OF RECORD

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

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