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ARTICLE

Cancer in General Responders Participating in World Trade Center Health Programs, 2003–2013

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Abstract

Background: Following the September 11, 2001, attacks on the World Trade Center (WTC), thousands of workers were exposed to an array of toxins known to cause adverse health effects, including cancer. This study evaluates cancer incidence in the WTC Health Program General Responder Cohort occurring within 12 years post exposure.
Methods: The study population consisted of 28 729 members of the General Responder Cohort enrolled from cohort inception, July 2002 to December 31, 2013. Standardized incidence ratios (SIRs) were calculated with cancer case inclusion and follow-up starting post September 11, 2001 (unrestricted) and, alternatively, to account for selection bias, with case inclusion and follow-up starting 6 months after enrollment in the WTC Health Program (restricted). Case ascertainment was based on linkage with six state cancer registries. Under the restricted criterion, hazard ratios were estimated using multivariable Cox proportional hazards models for all cancer sites combined and for prostate cancer.
Results: Restricted analyses identified 1072 cancers in 999 responders, with elevations in cancer incidence for all cancer sites combined (SIR = 1.09, 95% confidence interval [CI] = 1.02 to 1.16), prostate cancer (SIR = 1.25, 95% CI = 1.11 to 1.40), thyroid cancer (SIR = 2.19, 95% CI = 1.71 to 2.75), and leukemia (SIR = 1.41, 95% CI = 1.01 to 1.92). Cancer incidence was not associated with any WTC exposure index (composite or individual) for all cancer sites combined or for prostate cancer.
Conclusion: Our analyses show statistically significant elevations in cancer incidence for all cancer sites combined and for prostate and thyroid cancers and leukemia. Multivariable analyses show no association with magnitude or type of exposure.

Following the attacks on the World Trade Center (WTC) towers on September 11, 2001, more than 50 000 workers (1) were involved in rescue and recovery, with many of them caught directly in the dust cloud from the collapsing towers. The potential exposure of these workers extended until cleanup of the site ended in June 2002. The complex, sustained exposure and the unknown long-term health effects it may cause are matters of national concern and the subject of continued monitoring and research. Because of the presence of carcinogens (asbestos, polychlorinated biphenyls, benzene, dioxins) (2), several studies have examined cancer incidence among different WTC-exposed responder cohorts compared with the general population. A 10-year post–September 11 study by the WTC Health Registry of recovery workers and of people exposed in the vicinity of the WTC found a statistically significant greater incidence in all reportable, cancer registry types combined, with a standardized incidence ratio (SIR) of 1.11 (3). A study of 7-year post–September 11 cancer incidence among members of the WTC Health Program General Responder Cohort (eg, law enforcement, construction, telecommunication workers) found a 15%

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elevation in all-site cancer incidence (4,5). A study of New York City Fire Department (FDNY) firefighters found a slight, yet statistically significant, incidence elevation in all sites combined (6). However, a later study comparing the same cohort with other firefighters with similar occupational (but not WTC) exposures found no greater all-sites-combined incidence (7).

This article is an update of the earlier Solan et al. study (4) of the General Responder Cohort extending follow-up time by an additional 5 years, thereby increasing sample size and, given the longer latency for some cancers, the ability to detect associations between WTC exposure and cancer risk. Solan et al. used an unrestricted criterion, where cancer counts and person-years of observations began post September 11, and a restricted criterion, where both counts and person-years began 6 months after member enrollment in the WTC Health Program. When using the restricted approach, the earlier study found elevations in thyroid cancer only.

Cancer is now classified as a WTC-related condition by the National Institute for Occupational Safety and Health, and diagnosed members of the WTC Health Program are eligible for federally funded treatment. The General Responder Cohort is an open cohort, with new members enrolling as of the end date of this study (year 2013). Members have many reasons to enroll, including having a cancer certified for federally funded treatment. To reduce bias from sicker members disproportionately self-selecting into the program, we focused on the restricted criterion, excluding cancer cases and person-years of observation before the date of member enrollment plus 6 months. (For comparison with Solan et al. [before cancer was designated as WTC related], unrestricted criterion results are included as Supplementary Material, available online).

Methods

The WTC Health Program General Responder Cohort has been described in detail elsewhere (8). Briefly, the WTC Health Program is a federally funded medical monitoring and treatment program designed to assess responder health over time and to provide treatment for health conditions deemed WTC related. Human investigations are performed after approval by local institutional review boards and in accord with assurances filed with and approved by the US Department of Health and Human Services.

The study population included all members enrolled in the WTC Health Program General Responder Cohort between its inception (July 2002) and the end of follow-up (December 31, 2013, for New York residents and December 31, 2012, for residents of other states). To be included in these analyses, the following eligibility requirements pertained: self-reported time working on the WTC rescue and recovery effort was a 4-hour minimum in the first 4 days from September 11, 2001, 24 hours in September 2001, or 80 hours in September–December 2001; consent to have data aggregated for research; consent to have data shared with cancer registries; and completion of at least one monitoring visit (8).

Cancer cases were ascertained via linkage with the cancer registries of New York (NY) and surrounding states of New Jersey, Pennsylvania, and Connecticut, as well as Florida and North Carolina, where responders are known to retire. Cohort percentages living in these states at some point post September 11 were 87.7% (NY), 8.9% (New Jersey), 1.3% (Florida), 1.2% (Pennsylvania), 0.6% (Connecticut), and 0.3% (North Carolina). Linkages used probabilistic matching algorithms based on name, address, social security number (SSN), sex, race, and birth date. Registries use differing matching algorithms and degrees of manual review; false positive and false negative matches are possible, especially for those missing full SSN (full SSN was available for 31.8% of the study population and the last four SSN digits for an additional 15.1%). The NY registry performed an additional and extensive manual review of possible matches using Department of Motor Vehicle records and other sources.

The NY registry data are complete through December 31, 2013, and the others through December 31, 2012. Consequently, person-years based on responders' most recently reported state of residence were censored to December 31, 2013, for NY residents and to December 31, 2012, for residents of the five other states; residents of all other states were excluded from the analysis. Overlapping reporting of cancer among state registries was assessed via manual review; duplicates were removed to yield a dataset of unique registry-reported cancer cases for analysis.

Cancer cases were grouped into an "all cancer sites combined" category and into individual groupings per the National Cancer Institute's Surveillance, Epidemiology, and End Results site recode classifications (https://seer.cancer.gov/siterecode/icdo3_dwhoheme/index.html).

WTC exposure indices were obtained via a structured exposure assessment interview and consisted of reported exposure to the dust cloud (direct, significant, some, none) combined with arrival time (first day on the effort between September 11 and September 14 inclusive, first day on the effort after September 14); cumulative days working on the WTC effort; and working directly on the debris pile at any time.

A four-level (low, medium, high, very high) composite of these exposure measures was also used (9) and defined as follows: Low- and medium-exposure groups consisted of those who were not directly in the dust cloud, with the low-exposure group also requiring fewer than 40 days working on the WTC effort and not having worked at any time on the debris pile. The high and very high groups consisted of those who were directly in the dust cloud, with the very high group also requiring 90 or more days working on the WTC effort and working at some point on the debris pile.

This study includes exposure assessment and demographic data from monitoring visits starting 2002 through December 31, 2013. The exposure assessment questionnaire was administered at members' initial monitoring visits only. Demographic information, smoking status, and member address were obtained at first visit and updated at subsequent monitoring visits; address information was also updated through outreach efforts by the WTC Health Program and by member communications with the program's phone bank. The average number of member visits was 4.3, and average time between visits was 1.9 years.

Statistical Analysis

To calculate SIRs, population rates were extracted using SEER*STAT software, and expected counts were derived through indirect standardization to the age, sex, race and/or ethnicity, diagnosis year, and residency-state-specific population rates. These calculations were performed for each year of observation and then summed so that members could be aged yearly. Residence state from a member's most recent monitoring visit was used for combining with external rates. Observed counts were extracted from our registry-confirmed cancer dataset.

Under the restricted criterion, person-years of observation and observed counts began 6 months after member enrollment through December 31, 2013, for NY residents and December 31, 2012, for everyone else. Based on a linkage with the National Death Index, deceased members were censored at date of death. Both external population rates and our observed counts can include multiple cancer primaries per person (ie, a member with two stomach cancer primaries and colon cancer would be counted twice in the calculation of the site-specific SIR for stomach cancer and once for colon cancer). The 95% confidence intervals (CIs) for the SIRs (not presented by sex because of small numbers) were calculated using standard methods (10).

For comparison with previous research (4), unrestricted SIRs were calculated by not limiting to 6 months' post enrollment (ie, follow-up time and cancer cases started September 11, 2001). To test the adequacy of the restricted criterion's 6-month threshold to fully account for bias from selective enrollment due to prediagnosis symptoms of cancer, SIRs were calculated as a sensitivity analysis, with follow-up time and case inclusion beginning 12 and 24 months postenrollment.

To address potential confounders and explore the effects of WTC exposure and demographic variables on cancer risk, hazard ratios (HR) and 95% CIs were estimated using multivariable Cox proportional hazards models. Estimations were calculated separately for all cancer sites combined and for prostate cancer, with censoring at date of death, end-of-study, or cancer diagnosis date. No violations of the proportional hazards assumption were observed when tested using Schoenfeld residuals. We modeled multiple cancer events per member by using a shared frailty model, with subject treated as a gamma-distributed random effect to account for within-subject correlations among cancer event times (11). The time scale for the model was calendar time from September 11, 2001, but entry into the model was left-truncated at 6 months' postenrollment, per our restricted criterion. In addition to the four-level exposure metric, the model included race and/or ethnicity, WTC Health Program clinic, sex, age on September 11, 2001 smoking status, pre–September 11 occupation, presence of SSN for registry matching, and enrollment date. These known and suspected cancer risk factors are consistent with Solan et al. (4) and control for the heterogeneous nature of the types of responders in our cohort. A separate model, using the same covariates but substituting the three primary exposure indices for the four-level derived indices, was also examined. All models used the restricted criterion.

Results

Demographics

Of the 29 455 responders with appropriate consents and whose information was provided to the cancer registries for linkage, 726 were excluded because their restricted criterion start date (enrollment date + 6 months) occurred after the end date of available registry data or after their date of death, leaving an analysis sample size of 28 729.

The 28 729 responders were predominantly male (85.5%), white non-Hispanic (47.4%) with a median age of 38 years on September 11, 2001 (Table 1). Construction and protective services (eg, law enforcement) were the most common pre–September 11 occupations (20.8% and 49.0%, respectively), and 44.4% had at least some level of exposure to the dust cloud caused by the collapse of the WTC towers. The median time spent working on the rescue and recovery effort was 52 days.

Table 1. Selected characteristics of the World Trade Center Health Program General Responder study sample (N = 28 729)*

Characteristic	No. (%)
Sex	
Male	24 568 (85.52)
Female	4161 (14.48)
Median age on 9/11/2001, y	38
Race/ethnicity	
Black	3068 (10.68)
White non-Hispanic	13 620 (47.41)
White Hispanic	534 (1.86)
Hispanic (missing race)	4622 (16.09)
Other race	1938 (6.75)
Unknown/missing	4947 (17.22)
Occupation	
Protective services	14 087 (49.03)
Construction	5975 (20.80)
CM&IRG	2636 (9.18)
Other	6031 (20.99)
Smoking history	
Current	4290 (14.93)
Former	7069 (24.61)
Never	17 125 (59.61)
Missing	245 (0.85)
Clinical center at time of first visit	
Bellevue	1313 (4.57)
Mount Sinai Hospital	19 503 (67.89)
Queens	2149 (7.48)
Stony Brook	4561 (15.88)
Rutgers	1203 (4.19)
Derived exposure level	
Very high	920 (3.20)
High	4896 (17.04)
Intermediate	17 479 (60.84)
Low	4120 (14.34)
Missing	1314 (4.57)
Dust exposure/arrival time	
Direct dust exposure	5876 (20.45)
Significant dust exposure	4822 (16.78)
Some dust exposure	2046 (7.12)
No exposure/arrival 9/11–9/14	8480 (29.52)
No exposure/arrival after 9/14	6400 (22.28)
Missing	1105 (3.85)
Duration on effort, d	
1st quartile, 1–17	7161 (24.93)
2nd quartile, 18–52	6788 (23.63)
3rd quartile, 53–114	7096 (24.70)
4th quartile, >114	6987 (24.32)
Missing	697 (2.43)
Worked on pile/pit	
Yes	10 188 (35.46)
No	17 636 (61.39)
Missing	905 (3.15)
SSN full or partial sent to registry	
Yes	13 462 (46.86)
No	15 267 (53.14)
Date of enrollment	
2002–2005	14 141 (49.22)
2006–2009	10 513 (36.59)
2010–2013	4075 (14.18)

*CM&IRG = buildings and grounds cleaning and maintenance and electrical, telecommunications and other installation and repair groups; SSN = social security number.

Table 2. Standardized incidence ratios (SIRs) of selected cancers among World Trade Center Health Program General Responders, 2003–2013*: restricted criterion

Site	Observed	Expected	SIR (95% CI)	Median time 9/11/01 to cancer diagnosis, y
All cancer sites combined	1072	984.4	1.09 (1.02 to 1.16)	8.6
Smoking-related†	300	304.9	0.98 (0.88 to 1.10)	8.9
Oral cavity and pharynx	34	35.3	0.96 (0.67 to 1.34)	8.3
Digestive system	163	180.2	0.90 (0.77 to 1.05)	8.6
Esophagus	19	13.0	1.46 (0.88 to 2.28)	8.2
Stomach	19	17.8	1.07 (0.64 to 1.67)	8.3
Colon and rectum	68	84.0	0.81 (0.63 to 1.03)	7.8
Liver and intrahepatic bile duct	24	25.2	0.95 (0.61 to 1.42)	9.2
Pancreas	18	23.0	0.78 (0.46 to 1.24)	9.7
Nose, nasal cavity, and middle ear	<5	—	1.14	8.5
Larynx	10	12.0	0.83 (0.40 to 1.53)	9.8
Lung and bronchus	80	96.2	0.83 (0.66 to 1.04)	9.2
Soft tissue including heart	7	7.9	0.88 (0.35 to 1.82)	5.2
Melanoma of the skin	50	43.3	1.15 (0.86 to 1.52)	8.6
Breast	47	50.3	0.94 (0.69 to 1.24)	8.8
Corpus uteri	8	9.8	0.82 (0.35 to 1.61)	9.6
Prostate	298	238.7	1.25 (1.11 to 1.40)	8.6
Testis	10	14.5	0.69 (0.33 to 1.27)	5.9
Urinary bladder	48	44.2	1.09 (0.80 to 1.44)	9.3
Kidney and renal pelvis	54	46.7	1.16 (0.87 to 1.51)	9.2
Brain and other nervous system	21	15.6	1.34 (0.83 to 2.05)	8.6
Thyroid	73	33.4	2.19 (1.71 to 2.75)	8.7
Hematological	106	100.6	1.05 (0.86 to 1.27)	8.4
Hodgkin lymphoma	7	8.4	0.83 (0.34 to 1.72)	6.5
Non-Hodgkin lymphoma	47	48.8	0.96 (0.71 to 1.28)	8.5
Myeloma	12	15.0	0.80 (0.41 to 1.40)	8.3
Leukemia	40	28.4	1.41 (1.01 to 1.92)	8.5
CLL	12	11.1	1.08 (0.56 to 1.89)	8.7
AML	12	7.6	1.58 (0.82 to 2.76)	8.0
Mesothelioma	<5	—	1.25	6.5

*Begins 6 months past member enrollment, with enrollment beginning July 2002. AML = acute myeloid leukemia; CI = confidence interval; CLL = chronic lymphocytic leukemia.

†Smoking-related cancers consist of the following cancer types: oral cavity and pharynx (excluding nasopharynx), esophagus, liver, intrahepatic bile duct, pancreas, respiratory system (excluding pleura), urinary system, and acute myeloid leukemia.

SIR Results

Restricted Analyses

1072 cancers were identified among 999 responders. All cancer sites combined showed a statistically significant elevation in incidence (SIR = 1.09, 95% CI = 1.02 to 1.16) (Table 2), driven mostly by elevations in incidences of prostate cancer (SIR = 1.25, 95% CI = 1.11 to 1.40) and thyroid cancer (SIR = 2.19, 95% CI = 1.71 to 2.75). In contrast to Solan et al. (4), the incidence of leukemia was statistically significantly elevated (SIR = 1.41, 95% CI = 1.01 to 1.92). For esophageal and brain cancers, elevated incidence of 46% and 34%, respectively, were observed, but neither achieved statistical significance. Lung cancer showed a decreased SIR (0.83, 95% CI = 0.66 to 1.03) that was not statistically significant, as did colorectal cancer (SIR = 0.81, 95% CI = .63 to 1.03).

Unrestricted Analyses

The unrestricted criterion yielded statistically significant elevations in SIRs for all cancer sites combined, and with melanoma of the skin, prostate, bladder, kidney and thyroid cancers, hematologic neoplasms, leukemia, non-Hodgkin lymphoma, multiple myeloma, and chronic lymphocytic leukemia.

12- and 24-Month Restricted Sensitivity Analyses

Twelve- and 24-month sensitivity analyses were performed (Supplementary Table 1, available online). As with the 6-month restricted analysis, prostate cancer maintained statistically significant elevations in cancer incidence for both the 12-month (SIR = 1.23, 95% CI = 1.09 to 1.38) and the 24-month (SIR = 1.21, 95% CI = 1.06 to 1.37) restricted criteria. Likewise, thyroid cancer maintained a statistically significant elevation in cancer incidence for both the 12-month criterion (SIR = 2.18, 95% CI = 1.70 to 2.76) and the 24-month criterion (SIR = 2.11, 95% CI = 1.61 to 2.72). All cancer sites combined maintained a statistically significant elevation for the 12-month criterion (SIR = 1.07, 95% CI = 1.01 to 1.14) and borderline statistical significance for the 24-month criterion (SIR = 1.06, 95% CI = 0.99 to 1.13). The incidence of leukemia was no longer elevated, although results were based on diminishing numbers of cases.

Multivariable Analysis

Exposure Indices

None of the three separate exposure measures (dust exposure and arrival time, length of work time, or work on the pile) and none of the levels of the derived, four-level WTC exposure index

displayed a statistically significant association with cancer risk, for both all cancer sites combined and prostate cancer (Table 3).

Demographic and Other Variables

The multivariable analysis of all cancer sites combined (Table 3) suggested an elevated risk for men, compared with women, but the association did not achieve statistical significance (HR = 1.21, 95% CI = 0.97 to 1.52). Age on September 11, 2001, showed a statistically significant elevation of cancer risk, with a 1.09-fold greater risk for each 1-year increase (HR = 1.09, 95% CI = 1.08 to 1.10), and being a current smoker likewise showed a statistically significant association, with a 1.29-fold greater cancer risk compared with being a never smoker (HR = 1.29, 95% CI = 1.07 to 1.57). Being a former smoker was not associated with having an elevated cancer risk compared with being a never smoker (HR = 1.0, 95% CI = 0.85 to 1.17).

In the multivariable analysis of prostate cancer (Table 3), age on September 11, 2001, was statistically significant and was associated with a 1.13-fold greater cancer risk for each 1-year increase (HR = 1.13, 95% CI = 1.12 to 1.14); current and former smokers were associated with lower cancer risk compared with never smokers (HR = 0.74, 95% CI = 0.50 to 1.10, and HR = 0.94, 95% CI = 0.73 to 1.21, respectively).

Supplemental Multivariable Results

To test the adequacy of a 6-month threshold to account for selection bias, 12- and 24-month multivariable sensitivity analyses were performed (Supplementary Table 2, available online). Age on September 11, 2001, and current smoking status showed statistically significant associations with increased cancer risk for all cancer sites combined.

Discussion

Under the restricted criterion, we found statistically significant elevations in SIRs for all cancer sites combined, prostate and thyroid cancers, and leukemia; SIRs for lung cancer and colorectal cancer were below 1.0. Multivariable survival analysis showed no exposure dose-response for all cancer sites combined or prostate cancer, although some risk factors such as age at September 11, 2001, sex, and current smoking were associated with increased cancer risk. These analyses are most comparable in methodology with the previous restricted only analysis of Solan et al. (4), which had 5 fewer observation years, a smaller sample size, and wherein, an elevated SIR was reported for thyroid cancer only.

Solan et al. found elevations under the unrestricted criterion for all-sites cancer and prostate, thyroid, and hematologic malignancies and an elevation in soft tissue cancer, no longer evident in the current study. The current study found elevations under the unrestricted criterion in those same sites and many others (Supplementary Table 1, available online). Increased self-selection by a sicker subset of the overall responder population, due to both cancer becoming eligible for federally funded treatment and publicity from previous research on cancer risk among WTC-exposed populations, could explain these increases.

Although other studies have revealed elevated SIRs for other hematologic malignancies, this is the first reported statistically significant elevated SIR for leukemia (3,4,6,7). Leukemia is known to occur after exposure to occupational carcinogens, including benzene [burning jet fuel and other sources at the WTC site (12)], possibly at low levels of exposure (13,14) and with a latency of several years from exposure (15). Our study did not find an increase in multiple myeloma, as suggested by other studies (16,17), although all results are based on a small number of cases; thus, variation among studies is not surprising. Although we did not find an increase in multiple myeloma, continued surveillance is warranted, as a study of FDNY firefighters

Table 3. Hazard ratios of select exposure and demographic factors: multivariate Cox model of cancer risk for all cancer sites combined (men and women) and prostate cancer (men only)*

Factors	All cancer sites combined HR (95% CI)	Prostate HR (95% CI)
Sex†		
Male	1.21 (0.97 to 1.52)	—
Female	1.0 (Referent)	—
Age on 9/11/01,† y		
Per year	1.09 (1.08 to 1.10)	1.13 (1.12 to 1.14)
Occupation†		
Construction	1.12 (0.92 to 1.36)	1.22 (0.90 to 1.66)
Protective services	1.03 (0.84 to 1.26)	1.09 (0.77 to 1.56)
CM&IRG	0.96 (0.74 to 1.24)	1.15 (0.76 to 1.74)
All other	1.00 (Referent)	1.00 (Referent)
Smoking†		
Current smoker	1.29 (1.07 to 1.57)	0.74 (0.50 to 1.10)
Former smoker	1.00 (0.85 to 1.17)	0.94 (0.73 to 1.21)
Never smoked	1.00 (Referent)	1.00 (Referent)
SSN†,‡		
SSN sent to registry	0.95 (0.81 to 1.11)	1.08 (0.84 to 1.40)
No SSN sent	1.00 (Referent)	1.00 (Referent)
Derived exposure level§		
Low	1.00 (Referent)	1.00 (Referent)
Medium	0.91 (0.75 to 1.11)	0.82 (0.60 to 1.12)
High	0.99 (0.78 to 1.26)	0.93 (0.64 to 1.36)
Very high	0.67 (0.40 to 1.12)	0.48 (0.17 to 1.33)
Dust exposure/arrival time†		
Direct	1.07 (0.86 to 1.33)	1.18 (0.82 to 1.69)
Significant	1.16 (0.93 to 1.46)	1.43 (0.99 to 2.06)
Some	0.86 (0.62 to 1.20)	0.93 (0.52 to 1.66)
No exposure/arrival 9/11–9/14	1.06 (0.88 to 1.29)	1.11 (0.80 to 1.54)
No exposure/arrival after 9/14	1.00 (Referent)	1.00 (Referent)
Duration on site†		
1st quartile	1.00 (Referent)	1.00 (Referent)
2nd quartile	1.08 (0.88 to 1.32)	1.13 (0.82 to 1.55)
3rd quartile	0.99 (0.80 to 1.21)	0.83 (0.59 to 1.16)
4th quartile	1.04 (0.85 to 1.26)	0.82 (0.60 to 1.14)
Worked on pile†		
Yes	1.02 (0.88 to 1.19)	0.95 (0.74 to 1.22)
No	1.00 (Referent)	1.00 (Referent)

*CI = confidence interval; CM&IRG = buildings and grounds cleaning and maintenance and electrical, telecommunications, and other installation and repair groups; HR = hazard ratio; SSN = social security number.
†HRs from a model that included age on 9/11/01, sex, race and/or ethnicity, clinic, smoking, SSN status, year of registration, occupation, work on pile, duration on site, and dust exposure/arrival time.
‡SSN information sent to registry and used in probabilistic matching included both full SSN and last four digits.
§HRs from a model that included age, sex, race and/or ethnicity, clinic, smoking, SSN status, year of registration, occupation, and derived exposure level.

found a statistically significant association between WTC exposure and the myeloma precursor monoclonal gammopathy of undetermined significance (18).

Lung cancer is commonly associated with occupational exposures, and WTC debris contained substances known to increase lung cancer risk (asbestos, particulate matter), yet we found the SIR of this cancer to be below 1.00, albeit of borderline statistical significance (SIR = 0.83, 95% CI = 0.66 to 1.04). Three considerations for this finding are as follows: Our cohort has a lower prevalence of smokers compared with the general population; many members are certified with WTC-related musculoskeletal conditions, commonly treated with nonsteroidal, anti-inflammatory drugs for pain management that have been shown to decrease lung cancer risk (19); and latency might be a greater factor for lung cancer than for other cancers. These questions should be examined in future studies.

Routine screening for thyroid cancer is not offered through the WTC Health Program; however, General Responder Cohort members are routinely administered chest x-rays, and those with certain respiratory problems are administered chest computerized tomography scans, which can lead to early diagnosis of thyroid cancer. Consequently, medical surveillance could partially explain elevations in the thyroid cancer SIR.

An increase in prostate cancer among WTC-exposed firefighters has been reported, although surveillance bias may play a role, given that prostate-specific antigen screenings are routinely performed as part of the FDNY monitoring program (7) (the WTC Health Program does not screen for prostate cancer). Typical latency for prostate cancer has been estimated as long as 20 years post exposure (20); however, recent research suggests that respiratory exposure to WTC dust could induce inflammatory and immune responses in prostate tissue and that WTC-related prostate cancer displays a distinct gene expression pattern that could have resulted from exposure to specific carcinogens (21). These factors could be associated with a shorter latency period for WTC exposure.

Cancers commonly treated in outpatient settings may be underreported to registries, particularly melanoma and myeloid leukemia (22,23). Consequently, underreporting of cancer is a possible source of incomplete case ascertainment in our cohort. However, such undercounting would also affect the population rates used in SIR calculations and presumably would be nondifferential with respect to the exposure variables used in our multivariable analyses, leading to loss of power but not bias. Another potential source of undercounting would be missing SSN information in 68.2% of our cohort, because SSN is an important part of the probabilistic matching algorithms employed by the registries. Because of a renewed effort to collect the last four digits of SSN, this current study was able to provide the registries with partial SSN numbers on an additional 4331 responders, improving match accuracy and reducing potential undercounting. Based on a comparison of the registry linkage results on 5627 members initially without SSN with their updated results with the inclusion of the last four digits of SSN (4331 members) or the full SSN (1296 members), we can estimate registry matching without SSN results in an undercounting of true cancer numbers by 7.9% compared to full SSN and 5.4% *cf* last four digits.

Although Solan et al. (4) reported a non-statistically significant suggestion of an exposure dose-response, our analysis found no exposure effect, regardless of whether component or derived measures were examined. A more recent FDNY study (7) compared cancer incidence in their cohort to firefighters from other cities. Although our analysis used internal WTC-exposure comparisons whereas the firefighter study used an external control group, the firefighter study likewise reported no WTC exposure effect.

Days and hours on-site, location, and dust cloud exposure have been assumed surrogates for duration and intensity of exposure to cancer-causing substances. However, it is possible that these categories do not completely capture the true level of exposures to carcinogens. Similarly, use of respirators and protective clothing may mitigate the effects of exposure. Unfortunately, however, this information was not consistently captured via the exposure assessment instrument. Recall bias may also play a role among those who enrolled up to a decade or more after exposure, although the percentage of late enrollees remains small (14.2% after 2009). These potential limitations may result in exposure misclassification, reducing our ability to identify a dose-response effect, if one exists.

In conclusion, our investigation identified elevated incidence rates in all-sites cancer combined, as well as in prostate, thyroid, and leukemia when compared to the general population. However, no dose-response association was observed between cancer risk and estimated level of exposure while working on the WTC rescue and recovery effort. Shorter latency prostate cancer elevations could be contributed to the unique makeup of the WTC dust exposure. Future studies of other WTC-exposed cohorts may similarly find elevations in leukemia. Thyroid cancer continues to show the greatest elevations in SIR, possibly because of surveillance bias from increased monitoring and treatment, although thyroid cancer screening is not offered through the WTC Health Program. Because of the long latency period of many types of cancer, it is possible that increased rates of other cancers, as well as WTC exposure-cancer associations, may emerge after longer periods of follow-up.

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Notes

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