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Association Between World Trade Center Exposure and Excess Cancer Risk

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Context The terrorist attacks of September 11, 2001, resulted in the release of known and suspected carcinogens into the environment. There is public concern that exposures may have resulted in increased cancers.

Objective To evaluate cancer incidence among persons enrolled in the World Trade Center Health Registry.

Design, Setting, and Participants Observational study of 55 778 New York State residents enrolled in the World Trade Center Health Registry in 2003-2004, including rescue/recovery workers (n=21 850) and those not involved in rescue/recovery (n=33 928), who were followed up from enrollment through December 31, 2008. Within-cohort comparisons using Cox proportional hazards models assessed the relationship between intensity of World Trade Center exposure and selected cancers.

Main Outcome Measures Cases were identified through linkage with 11 state cancer registries. Standardized incidence ratios (SIRs) adjusted for age, race/ethnicity, and sex were computed with 2003-2008 New York State rates as the reference, focusing on cancers diagnosed in 2007-2008 as being most likely to be related to exposure during September 11 and its aftermath. The total and site-specific incidence rate differences (RDs) per 100 000 person-years between the study population and the New York State population in 2007-2008 also were calculated.

Results There were 1187 incident cancers diagnosed, with an accumulated 253 269 person-years (439 cancers among rescue/recovery workers and 748 among those not involved in rescue/recovery). The SIR for all cancer sites combined in 2007-2008 was not significantly elevated (SIR, 1.14 [95% CI, 0.99 to 1.30]; RD, 67 [95% CI, −6 to 126] per 100 000 person-years among rescue/recovery workers vs SIR, 0.92 [95% CI, 0.83 to 1.03]; RD, −45 [95% CI, −106 to 15] per 100 000 person-years among those not involved in rescue/recovery). Among rescue/recovery workers, the SIRs had significantly increased by 2007-2008 for 3 cancer sites and were 1.43 (95% CI, 1.11 to 1.82) for prostate cancer (n=67; RD, 61 [95% CI, 20 to 91] per 100 000 person-years), 2.02 (95% CI, 1.07 to 3.45) for thyroid cancer (n=13; RD, 16 [95% CI, 2 to 23] per 100 000 person-years), and 2.85 (95% CI, 1.15 to 5.88) for multiple myeloma (n=7; RD, 11 [95% CI, 2 to 14] per 100 000 person-years). No increased incidence was observed in 2007-2008 among those not involved in rescue/recovery. Using within-cohort comparisons, the intensity of World Trade Center exposure was not significantly associated with cancer of the lung, prostate, thyroid, non-Hodgkin lymphoma, or hematological cancer in either group.

Conclusions Among persons enrolled in the World Trade Center Health Registry, there was an excess risk for prostate cancer, thyroid cancer, and myeloma in 2007-2008 compared with that for New York State residents; however, these findings were based on a small number of events and multiple comparisons. No significant associations were observed with intensity of World Trade Center exposures. Longer follow-up for typically long-latency cancers and attention to specific cancer sites are needed.

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THE TERRORIST ATTACKS ON THE World Trade Center (WTC) on September 11, 2001, claimed more than 2700 lives and exposed hundreds of thousands of people to dust, debris, pulverized building materials, and potentially toxic emissions, resulting in short- and medium-term health effects.[1-6] The dust, smoke, and aerosols were complex mixtures of volatile chemicals and respirable particulate matter less than 2.5 μm in diameter and contained known and suspected carcinogens including asbestos, silica, benzene, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, volatile organic compounds, and numerous metals.[7-10]

The presence of carcinogenic agents raises the possibility that exposure to the WTC environment could eventually lead to cancers. Thus far, the only systematic examination of cancer incidence is a study of 9853 male firefighters employed by the Fire Department of the City of New York (FDNY).[11] Zeig-Owens et al[11] reported 19% excess incidence for all cancer sites combined among WTC-exposed firefighters com-

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pared with unexposed firefighters in the 7 years following September 11. Most of the excess incidence was composed of prostate and thyroid cancers, non-Hodgkin lymphoma, and melanoma. A mortality study from the WTC Health Registry, in which 41 930 WTC-exposed New York City residents were followed up through 2009, found that the total mortality from potentially short incubation and fatal hematological malignancies did not differ significantly from expected.[12] However, the follow-up period was short relative to the onset and survival times for most cancers.

We evaluated cancer incidence to determine any excess cancer among rescue/recovery workers and volunteers and those not involved in rescue/recovery enrolled in the registry, laying the groundwork for periodic cancer surveillance.

METHODS

Study Population

The World Trade Center Health Registry is a cohort study designed to monitor the health effects of the September 11 attacks among rescue/recovery workers and persons who lived, worked, or attended school in lower Manhattan. The study methods have been published elsewhere.[2,13] Briefly, in 2003-2004 a total of 71 434 persons completed a telephone (95%) or in-person (5%) interview. Participants were either identified through lists provided by employers, government agencies, and other entities (30%; list identified) or they responded to an outreach campaign (70%; self-identified). Coverage of the eligible population was estimated as 34% for rescue/recovery workers and 23% for residents.[14] Verbal informed consent was obtained from each of the participants. This analysis included registry enrollees who were New York State (NYS) residents on September 11 and at risk for a first primary invasive cancer at the time of registry enrollment, defined as never having had a primary invasive cancer documented in any of the 11 state cancer registries we used for case identification.

This study was approved by the institutional review board of the New York City Department of Health and Mental Hygiene. Each cancer registry record linkage was also approved by the respective institutional review board of 10 state departments of health listed below and the University of Medicine and Dentistry of New Jersey.

Outcome Definition

Cancers were identified through record linkage with 11 state cancer registries. Eligible study participants were matched to cancer registries that have been population based since 1976 (in NYS) and 1978 (in New Jersey). Residents of NYS on September 11 who later moved to California, Connecticut, Florida, North Carolina, Massachusetts, Ohio, Pennsylvania, Texas, or Washington were matched to the corresponding state cancer registry. The proportion of the cancer cases with a full or partial social security number was similar to that in noncancer cases (76.1% vs 76.5%, respectively; $P = .78$). An incident cancer case is defined as a first primary invasive cancer or in situ bladder cancer matched to a state cancer registry and diagnosed any time postenrollment through December 31, 2008, the last date for which complete cancer incidence records were available for observed and expected cancer computations. Cancer site was defined using the Surveillance, Epidemiology, and End Results (SEER) site recode *International Classification of Diseases for Oncology, Third Edition,* grouping, in which categories are based on primary site and histology.[15]

Exposure to WTC and Covariates

Demographic and exposure data were obtained at registry enrollment. Rescue/recovery workers were first responders, volunteers, and others who worked at the WTC site, debris-loading sites, on barges, or at the Staten Island landfill between September 11, 2001, and June 30, 2002. Participants not involved in rescue/recovery were residents, children, and staff in schools (prekindergarten-12th grade) south of Canal Street and area workers and passersby south of Chambers Street on September 11 in lower Manhattan. Persons belonging to both groups were categorized as rescue/recovery workers.

Separate qualitative descriptions of WTC exposures were used to classify exposure as high, intermediate, or low for rescue/recovery workers (excluding those who worked exclusively on Staten Island) and for participants not involved in rescue/recovery (exposure level definitions appear in the eTable at http://www.jama.org). Highly exposed rescue/recovery workers were in the immediate area at the time of the WTC towers' collapse and worked on the dust and debris pile on September 11 or worked at the site for more than 90 days starting in the first week after September 11. Highly exposed participants not involved in rescue/recovery reported 2 or more injuries on September 11, and resided or worked in lower Manhattan and did not evacuate or were present at school on September 11.[12] Rescue/recovery workers and those not involved in rescue/recovery generally experienced qualitatively different exposures, and were therefore analyzed separately. Covariates included age at enrollment, sex, race/ethnicity, 2002 household income level, education level, smoking status, enrollment source (list identified or self-identified), and history of asthma, cardiovascular disease, stroke, emphysema, or diabetes reported at enrollment.

Data Analyses

We compared the cancer experience of each group with the NYS population using the standardized incidence ratio (SIR), computed as the ratio of observed to expected cancer cases, stratified by age (5-year age groups), race/ethnicity, sex, and calendar period (2003-2006 and 2007-2008). We used NYS cancer rates to determine expected cases because the study population was only NYS residents on

September 11 and the NYS cancer registry was the source of all but 5% of study cases.

We constructed our analysis to increase the likelihood of detecting September 11 exposure–related cancer at this early stage of follow-up. A little more than 7 years elapsed between September 11 and the end of follow-up, which is less than the average latency period for most solid tumors. Nevertheless, short latency periods have been reported for cancers associated with exposure to chemicals in adults[16] and exposure to radiation in children.[17] We hypothesized that any exposure-related cancers would be more likely to emerge at least 5 years after September 11 and thus divided the follow-up interval into early (enrollment through 2006) and later (2007-2008) periods, and focused on cancers occurring in the later period.

We computed SIRs separately for the rescue/recovery workers and participants not involved in rescue/recovery, after excluding 1820 enrollees (61 cancers) with unknown ethnicity or unclassifiable race. Person-time of observation for each participant was calculated from the date of enrollment until the first cancer diagnosis, death, or December 31, 2008, whichever came first. The 95% confidence intervals of the SIRs were calculated using Byar approximation to the exact Poisson distribution.[18]

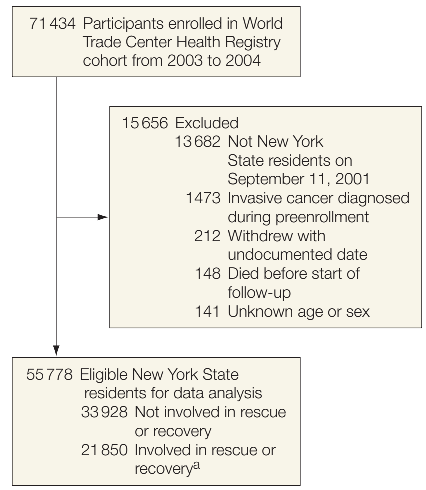
We also computed the rate differences (RDs) and 95% confidence intervals for the later period as the difference between the actual incidence rate per 100 000 person-years of the study population and the incidence rate in the NYS general population, adjusted by age, sex, race/ethnicity, and calendar-year time to the distribution of person-years in our study population. The statistical significance and 95% confidence intervals for the RDs were computed based on the assumption of a Poisson distribution. We did not adjust the *P* values for multiple comparisons.

Cancer sites with significantly elevated SIRs in the later period were selected for within-cohort comparisons during the entire follow-up period and were examined by exposure category using Cox proportional hazards models separately for rescue/recovery workers and participants not involved in rescue/recovery. Hematological cancers, which include myeloma, leukemia, and lymphoma, also were examined using the Cox model because each has a potentially shorter latency period compared with solid tumors and thus might be more likely to show an early increase. Additionally, lung cancer was included because the dust and debris from the WTC site contained silica, asbestos, and other carcinogens that have been associated with lung cancer. No violation of the proportional hazards assumption was observed for any model. Hazard ratios (HRs) and 95% confidence intervals were adjusted for age at enrollment, sex, race/ethnicity, smoking status, education level, income level, and history of a serious, nonmalignant medical condition as described above. Source of enrollment (self-identified vs list identified) was included in multivariate analyses to control for potential selection bias.

To account for a 5-year lag time from first WTC exposure, we reran the Cox models under the assumption that cancers diagnosed in the early period were unlikely to be caused by WTC exposures, thereby treating all study participants in the early period as if they were not exposed while retaining the originally assigned WTC exposure category in the later period.

Because we did not have data on the cancer screening practices of the participants, we indirectly assessed potential screening bias in 2 ways. First, we compared the number of stage I cancers for selected sites as a proportion of total cancer diagnoses in the study population with the corresponding proportion in the NYS population during the same period based on the assumption that screening-detected cancers are more likely to be early-stage cancers. Second, we compared the proportions of participants who reported a routine physical checkup within the preceding 12 months between those with and without subsequent cancers among all follow-up participants. Proportions were compared using the Pearson χ^2 test.

Figure. Selection of Study Population



[a]Of the 21 850 rescue/recovery workers, there were 21 371 who worked at the World Trade Center site and 479 who worked exclusively at the Staten Island recovery operation landfill or on transportation barges.

Descriptive and multivariate analyses were performed using SAS software version 9.2 (SAS Institute Inc), and SIRs were computed using SEER*Stat MP-SIR sessions software version 7.0.5 (http://www.seer.cancer.gov/seerstat). Significance was set at a 2-sided *P* value of less than .05.

RESULTS

This analysis was restricted to the 55 778 enrollees who were NYS residents on September 11 (78% of all registry enrollees) and at risk for a first primary invasive cancer at enrollment (FIGURE). We excluded enrollees with preenrollment invasive cancers (n=1473), those with unknown age or sex (n=141), and those who died before the start of follow-up (n=148) or withdrew with an undocumented date (n=212). Of the 55 778 enrollees, 90% remained in NYS throughout the follow-up period, 8% moved to states covered by the 10 state cancer registries mentioned earlier, and 2% moved elsewhere.

Through December 31, 2008, 1187 incident cancers were reported among the 55 778 eligible enrollees, with an accumulated 253 269 person-years. Of these 1187 cancers, 439 (37%) were diagnosed among rescue/recovery workers and 748 (63%) were among participants not involved in rescue/recovery.

Table 1. Characteristics of Rescue/Recovery Workers With and Without First Primary Incident Cancer During the Follow-up Period (n = 21 850)

	No. (%) of Rescue/Recovery Workers by First Primary Cancer Diagnosis During the Follow-up Period		
	Cancer Cases (n = 439)	No Cancer (n = 21 411)	*P* Value
Source of enrollment			
List identified	147 (33.5)	6495 (30.3)	.16
Self-identified	292 (66.5)	14 916 (69.7)	
Age at enrollment, y			
<20	0	69 (0.3)	<.001
20-34	20 (4.6)	4670 (21.8)	
35-44	73 (16.6)	8406 (39.3)	
45-64	313 (71.3)	7977 (37.3)	
≥65	33 (7.5)	289 (1.4)	
Sex			
Male	366 (83.4)	17 299 (80.8)	.18
Female	73 (16.6)	4112 (19.2)	
Race/ethnicity			
Non-Hispanic white	308 (70.2)	14 218 (66.4)	<.001
Non-Hispanic black	55 (12.5)	2353 (11.0)	
Hispanic	43 (9.8)	3463 (16.2)	
Asian	7 (1.6)	630 (2.9)	
American Indian or Alaska Native	8 (1.8)	133 (0.6)	
Unknown	18 (4.1)	614 (2.9)	
Education at enrollment			
<High school	38 (8.7)	1260 (5.9)	.02
High school	122 (27.8)	5454 (25.5)	
Some college	112 (25.5)	6729 (31.4)	
≥College degree	160 (36.4)	7682 (35.9)	
Unknown	7 (1.6)	286 (1.3)	
Household income in 2002, $			
<50 000	87 (19.8)	5137 (24.0)	.09
50 000-<150 000	274 (62.4)	13 183 (61.6)	
≥150 000	33 (7.5)	1249 (5.8)	
Unknown	45 (10.3)	1842 (8.6)	
Smoking status at enrollment			
Current	70 (15.9)	4010 (18.7)	<.001
Former	156 (35.7)	5559 (26.0)	
Never	207 (47.0)	11 603 (54.2)	
Unknown	6 (1.4)	239 (1.1)	
Preexisting medical condition[a]			
Yes	163 (37.1)	4467 (20.9)	<.001
No or unknown	276 (62.9)	16 944 (79.1)	
World Trade Center exposure level[b]			
Low	26 (5.9)	1456 (6.8)	.04
Intermediate	330 (75.2)	16 382 (76.5)	
High	58 (13.2)	2884 (13.5)	
Missing or unknown	6 (1.4)	229 (1.1)	
Worked exclusively at Staten Island site	19 (4.3)	460 (2.2)	

[a] Included asthma, cardiovascular disease, stroke, emphysema, or diabetes reported at enrollment.
[b] Exposure level definitions appear in the eTable at http://www.jama.com.

The median age at diagnosis across all cancer sites was 57 years (range, 22-103 years); none was diagnosed in persons younger than 20 years old. Characteristics of cancer cases and those without cancer are shown in TABLE 1 for rescue/recovery workers and in TABLE 2 for participants not involved in rescue/recovery. Participants diagnosed with cancer in both groups were significantly older, less likely to be Hispanic, and more likely to be ever smokers, and to have a prior history of medical conditions. The proportion who reported having a routine physical checkup within the preceding 12 months among those with subsequent cancer was not different from the proportion among those not diagnosed with cancer (72% vs 69%, respectively; $P=.17$).

Cancer Incidence Among Rescue/Recovery Workers

We excluded from the SIR analysis 632 rescue/recovery workers with unknown race/ethnicity, of whom 18 were cases. This left 421 cases for the SIR analysis. There were 198 cancers (47%) occurring in the early period and 223 (53%) in the later period. For all sites combined, cancer incidence was not significantly different from that in the reference population during either the early period (SIR, 0.94; 95% CI, 0.82 to 1.08) or the later period (SIR, 1.14; 95% CI, 0.99 to 1.30) (RD, 67 [95% CI, −5.5 to 126.2] per 100 000 person-years; TABLE 3).

Of the 23 cancer sites investigated, 3 had significantly elevated incidence during the later period: prostate (n=67; SIR, 1.43 [95% CI, 1.11-1.82]; RD, 61 [95% CI, 20.1-91.4] per 100 000 person-years), thyroid (n=13; SIR, 2.02 [95% CI, 1.07-3.45]; RD, 16 [95% CI, 2.1-22.6] per 100 000 person-years), and multiple myeloma (n=7; SIR, 2.85 [95% CI, 1.15-5.88]; RD, 11.1 [95% CI, 2.2-14.2] per 100 000 person-years). Of these 3, thyroid cancer also was significantly elevated during the early period (n=14; SIR, 2.22 [95% CI, 1.22-3.73]). Ovarian cancer was significantly elevated during the early period (n≤5;

SIR, 3.32 [95% CI, 1.08-7.74]) but not during the later period (no cases reported). Nonsignificant SIRs exceeding 2.0 were observed for Hodgkin lymphoma in both periods based on 5 cases or less in each period.

Firefighters enrolled in the registry may have been included in the study by Zeig-Owens et al.[11] We recalculated later period SIRs excluding 2965 (2888 males and 77 females) FDNY firefighters in the registry to address the possibility that annual cancer screening of firefighters might lead to earlier cancer diagnoses. After exclusion, the later period SIR for thyroid cancer decreased and became nonsignificant (n=10; SIR, 1.76 [95% CI, 0.85-3.24]), whereas the SIRs for prostate cancer (n=54; SIR, 1.35 [95% CI, 1.01-1.76]) and multiple myeloma (n=6; SIR, 2.79 [95% CI, 1.02-6.06]) remained significantly elevated.

A significantly reduced SIR was observed for lung cancer during the early period based on 11 observed cases (SIR, 0.49 [95% CI, 0.24 to 0.87]). The later period SIR for lung cancer was reduced but was not statistically significant (n=13; SIR, 0.65 [95% CI, 0.35 to 1.12]; RD, −17.2 [95% CI, −59.2 to 3.4] per 100 000 person-years). No mesothelioma cases were reported. Breast cancer among female rescue/recovery workers was significantly reduced during the early period (n=6; SIR, 0.40 [95% CI, 0.15 to 0.87]), but not during the later period.

Cancer Incidence Among Participants Not Involved in Rescue/Recovery

We excluded from the SIR analysis 1188 participants not involved in rescue/recovery with unkown race/ethnicity, of whom 43 were cases. This left 705 cases for the SIR analysis. There were 381 cancers (54%) in the early and 324 (46%) in the later period (TABLE 4). For all cancer sites combined, cancer incidence was not significantly different from the reference population during either the early (SIR, 0.92 [95% CI, 0.83 to 1.02]) or later period (SIR, 0.92 [95% CI, 0.83 to 1.03]; RD, −45.0 [95% CI, −106.1 to 15.1] per 100 000 person-years).

In the early period, the SIR for Hodgkin lymphoma was significantly higher than expected (n=8; SIR, 2.60 [95% CI, 1.12 to 5.13]) and colorectal cancer was significantly lower than expected (n=25; SIR, 0.64 [95% CI, 0.42 to 0.95]). Both cancers were nonsignificant in the later period with the SIR for

Table 2. Characteristics of Participants Not Involved in Rescue/Recovery With and Without First Primary Incident Cancer During the Follow-up Period (n = 33 928)

	No. (%) of Participants Not Involved in Rescue/Recovery by First Primary Cancer Diagnosis During Follow-up Period		
	Cancer Cases (n = 748)	No Cancer (n = 33 180)	*P* Value
Source of enrollment			
List identified	198 (26.5)	7833 (23.6)	.07
Self-identified	550 (73.5)	25 347 (76.4)	
Age at enrollment, y			
<20	0	2954 (8.9)	<.001
20-34	28 (3.7)	7743 (23.3)	
35-44	84 (11.2)	8025 (24.2)	
45-64	475 (63.5)	12 571 (37.9)	
≥65	161 (21.5)	1887 (5.7)	
Sex			
Male	336 (44.9)	14 670 (44.2)	.70
Female	412 (55.1)	18 510 (55.8)	
Race/ethnicity			
Non-Hispanic white	441 (59.0)	17 927 (54.0)	<.001
Non-Hispanic black	118 (15.8)	5153 (15.5)	
Hispanic	66 (8.8)	4734 (14.3)	
Asian	77 (10.3)	4102 (12.4)	
American Indian or Alaska Native	3 (0.4)	119 (0.4)	
Unknown	43 (5.8)	1145 (3.5)	
Education at enrollment			
<High school	67 (9.0)	4274 (12.9)	.002
High school	124 (16.6)	4777 (14.4)	
Some college	158 (21.1)	6143 (18.5)	
≥College	381 (50.9)	17 460 (52.6)	
Unknown	18 (2.4)	526 (1.6)	
Household income in 2002, $			
<50 000	256 (34.2)	12 026 (36.2)	.02
50 000-<150 000	291 (38.9)	12 553 (37.8)	
≥150 000	78 (10.4)	4238 (12.8)	
Unknown	123 (16.4)	4363 (13.1)	
Smoking status at enrollment			
Current	120 (16.0)	4788 (14.4)	<.001
Former	275 (36.8)	7683 (23.2)	
Never	337 (45.1)	18 729 (56.4)	
Unknown	16 (2.1)	1980 (6.0)	
Preexisting medical condition[a]			
Yes	335 (44.8)	8013 (24.2)	<.001
No or unknown	413 (55.2)	25 167 (75.8)	
World Trade Center exposure level[b]			
Low	347 (46.4)	16 054 (48.4)	.06
Intermediate	326 (43.6)	14 220 (42.9)	
High	57 (7.6)	2476 (7.5)	
Missing or unknown	18 (2.4)	430 (1.3)	

[a] Included asthma, cardiovascular disease, stroke, emphysema, or diabetes reported at enrollment.
[b] Exposure level definitions appear in the eTable at http://www.jama.com.

Hodgkin lymphoma dropping below 1 (n≤5; SIR, 0.48 [95% CI, 0.01 to 2.66]; RD, −1.7 [95% CI, −158.3 to 1.0] per 100 000 person-years). There were fewer observed lung cancer cases than expected during both periods.

Proportional Hazards Analyses

TABLE 5 shows the adjusted HRs (AHRs) by exposure level for selected cancers during the entire follow-up period. Multivariate analyses were not performed separately for myeloma, Hodgkin lymphoma, or leukemias due to very small numbers of cases. The exposure metric was not significantly associated with any individual cancer site for either group. For hematological cancers among rescue/recovery workers, the intermediate exposure AHR was 3.7, and the high exposure AHR was 4.5 compared with the low exposure level; however, neither the trend nor either AHR was significant (*P*=.20 for trend). When a 5-year lag time was introduced, the AHRs for hematological cancer were lower for both intermediate (AHR, 1.6 [95% CI, 0.8-3.0]) and high exposure (AHR, 1.5 [95% CI, 0.5-4.5]). All of the 95% confidence intervals in Table 5 included unity and were thus not statistically significant.

Table 3. Standardized Incidence Ratio (SIR) Adjusted for Age, Race/Ethnicity, and Sex and 2007-2008 Rate Difference of First Primary Cancer Site Among Rescue/Recovery Workers With Known Race/Ethnicity Using the New York State Population Rate as Reference (n = 21 218)

	Early Period (Enrollment Through 2006) (n = 21 218)[a]		Later Period (2007-2008) (n = 20 991)[b]		Incidence Rate per 100 000 Person-Years (2007-2008)		
Cancer Site	No. Observed[c]	SIR (95% CI)[d]	No. Observed[e]	SIR (95% CI)[d]	Rescue/ Recovery Workers	NYS Population	RD (95% CI) per 100 000 Person-Years
All first primary invasive malignant tumors	198	0.94 (0.82 to 1.08)	223	1.14 (0.99 to 1.30)	546.7	479.6	67.1 (−5.5 to 126.2)
Oral cavity and pharynx	8	1.13 (0.49 to 2.24)	≤5	0.77 (0.25 to 1.80)	12.3	15.9	−3.7 (−36.8 to 5.4)
Esophagus	≤5	1.43 (0.39 to 3.67)	≤5	1.16 (0.24 to 3.39)	7.4	6.3	1.0 (−23.3 to 5.2)
Stomach	≤5	0.52 (0.06 to 1.88)	≤5	0.91 (0.19 to 2.67)	7.4	8.1	−0.7 (−31.4 to 4.6)
Colorectal	15	0.80 (0.45 to 1.31)	21	1.24 (0.77 to 1.90)	51.5	41.5	10.0 (−15.4 to 24.4)
Liver and intrahepatic bile duct	≤5	0.43 (0.05 to 1.54)	6	1.22 (0.45 to 2.67)	14.7	12.1	2.7 (−18.0 to 9.2)
Pancreas	6	1.37 (0.50 to 2.97)	≤5	0.70 (0.14 to 2.03)	7.4	10.5	−3.2 (−45.2 to 3.7)
Larynx	≤5	1.76 (0.57 to 4.11)	0	0 (0 to 1.52)			
Lung and bronchus	11	0.49 (0.24 to 0.87)	13	0.65 (0.35 to 1.12)	31.9	49.0	−17.2 (−59.2 to 3.4)
Melanoma of the skin	14	1.61 (0.88 to 2.70)	10	1.32 (0.63 to 2.43)	24.5	18.6	5.9 (−14.4 to 14.4)
Female breast	6	0.40 (0.15 to 0.87)	18	1.39 (0.82 to 2.20)	231.9	166.9	65.1 (−50.9 to 126.5)
Cervix uteri	0	0 (0 to 2.67)	0	0 (0 to 3.45)			
Corpus uterus and not otherwise specified	≤5	0.97 (0.20 to 2.83)	0	0 (0 to 1.27)			
Ovary	≤5	3.32 (1.08 to 7.74)	0	0 (0 to 3.04)			
Prostate	48	1.12 (0.83 to 1.49)	67	1.43 (1.11 to 1.82)	202.8	141.9	61.0 (20.1 to 91.4)
Testis	≤5	0.75 (0.15 to 2.18)	≤5	0.36 (0.01 to 1.98)	3.0	8.4	−5.4 (−299.7 to 1.5)
Urinary bladder	9	0.96 (0.44 to 1.83)	8	0.94 (0.41 to 1.85)	19.6	20.9	−1.3 (−28.2 to 9.0)
Kidney and renal pelvis	6	0.68 (0.25 to 1.48)	12	1.38 (0.71 to 2.41)	29.4	21.3	8.1 (−12.0 to 17.2)
Brain and other nervous system	≤5	1.02 (0.28 to 2.62)	≤5	0.68 (0.08 to 2.45)	4.9	7.2	−2.3 (−56.4 to 2.9)
Thyroid	14	2.22 (1.22 to 3.73)	13	2.02 (1.07 to 3.45)	31.9	15.8	16.1 (2.1 to 22.6)
Hodgkin lymphoma	≤5	2.08 (0.68 to 4.86)	≤5	2.47 (0.67 to 6.31)	9.8	4.0	5.8 (−4.8 to 8.3)
Non-Hodgkin lymphoma	12	1.10 (0.57 to 1.92)	11	1.15 (0.57 to 2.06)	27.0	23.4	3.5 (−20.3 to 13.9)
Multiple myeloma	≤5	0.38 (0.01 to 2.11)	7	2.85 (1.15 to 5.88)	17.2	6.0	11.1 (2.2 to 14.2)
Leukemia	≤5	0.73 (0.20 to 1.87)	6	1.25 (0.46 to 2.72)	14.7	11.8	2.9 (−17.3 to 9.3)

Abbreviations: NYS, New York State; RD, rate difference.
[a] Analysis limited to the 21 218 rescue/recovery workers with known race/ethnicity.
[b] By the late period, of the 21 218 rescue/recovery workers with known race/ethnicity, 227 had been either diagnosed with cancer or died during the early period, and were therefore not eligible for inclusion in the late period analysis.
[c] Defined as the first primary cancers that were diagnosed between enrollment and December 31, 2006. All observed cancer cases were documented in the NYS cancer registry (n=192) and other state cancer registries (Florida=4, New Jersey=1, and Pennsylvania=1). Exact numbers not provided to comply with internal New York City Department of Health and Mental Hygiene and New York State cancer registry policies of not reporting small numbers.
[d] Expected cancers are based on 2003-2006 NYS incidence rates for the early period and 2007-2008 rates for the later period.
[e] Defined as the first primary cancers that were diagnosed between January 1, 2007, and December 31, 2008. All observed cancer cases were documented in the NYS cancer registry (n=209) and other state cancer registries (California=2, Connecticut=1, Florida=6, North Carolina=1, New Jersey=1, and Pennsylvania=3). Exact numbers not provided to comply with internal New York City Department of Health and Mental Hygiene and New York State cancer registry policies of not reporting small numbers.

COMMENT

Dust, debris, and fumes from the WTC contained known and suspected carcinogens, including polycyclic aromatic hydrocarbons, asbestos, benzene, and dioxins.[10,19-21] At issue is whether dosages to exposed individuals were sufficient to cause excess malignancies and, if so, whether such excesses are epidemiologically detectable at present. Also at issue is whether any specific cancer site with an observed excess might plausibly be related to September 11 exposure. In this early study with less than 8 years of follow-up, there was no statistically significant increased incidence for all cancer sites combined. Among rescue/recovery workers, however, multiple myeloma and prostate and thyroid cancers were significantly elevated in the later period. None of the cancers chosen for within-cohort comparisons (including the 3 with elevated SIRs) was associated with intensity of WTC exposure. The increase in hematological cancers with increasing exposure in rescue/recovery workers was not statistically significant.

Table 4. Standardized Incidence Ratio (SIR) Adjusted for Age, Race/Ethnicity, and Sex and 2007-2008 Rate Difference of First Primary Cancer Site Among Participants Not Involved in the Rescue/Recovery With Known Race/Ethnicity Using New York State Population Rate as Reference (n = 32 740)

	Early Period (Enrollment Through 2006) (n = 32 740)[a]		Later Period (2007-2008) (n = 32 216)[b]		Incidence Rate per 100 000 Person-Years (2007-2008)		
Cancer Site	No. Observed[c]	SIR (95% CI)[d]	No. Observed[e]	SIR (95% CI)[d]	Not Involved in Rescue/Recovery	NYS Population	RD (95% CI) per 100 000 Person-Years
All first primary invasive malignant tumors	381	0.92 (0.83 to 1.02)	324	0.92 (0.83 to 1.03)	518.0	563.1	−45.0 (−106.1 to 15.1)
Oral cavity and pharynx	10	1.03 (0.49 to 1.89)	6	0.73 (0.27 to 1.60)	9.6	13.1	−3.5 (−25.9 to 3.6)
Esophagus	≤5	0.24 (0.01 to 1.36)	≤5	0.29 (0.01 to 1.59)	1.6	5.5	−3.9 (−158.3 to 0.6)
Stomach	≤5	0.49 (0.13 to 1.25)	≤5	0.31 (0.04 to 1.11)	3.2	10.3	−7.1 (−76.7 to 0.3)
Colorectal	25	0.64 (0.42 to 0.95)	23	0.75 (0.47 to 1.12)	36.8	49.0	−12.3 (−41.5 to 3.9)
Liver and intrahepatic bile duct	≤5	0.67 (0.22 to 1.57)	9	1.30 (0.59 to 2.47)	14.4	11.1	3.3 (−10.0 to 8.6)
Pancreas	9	0.99 (0.45 to 1.88)	8	0.99 (0.43 to 1.96)	12.8	12.9	−0.1 (−17.0 to 6.3)
Larynx	≤5	1.37 (0.45 to 3.20)	0	0 (0 to 1.25)			
Lung and bronchus	35	0.74 (0.52 to 1.03)	26	0.66 (0.43 to 0.95)	41.6	63.0	−21.4 (−55.1 to −2.2)
Melanoma of the skin	18	1.48 (0.88 to 2.35)	8	0.78 (0.33 to 1.53)	12.8	16.4	−3.6 (−24.8 to 4.4)
Female breast	84	1.19 (0.95 to 1.48)	69	1.20 (0.93 to 1.52)	197.9	164.9	33.0 (−14.9 to 67.7)
Cervix uteri	≤5	0.32 (0.04 to 1.16)	≤5	0.86 (0.23 to 2.21)	11.5	13.3	−1.9 (−38.4 to 6.3)
Corpus uterus and not otherwise specified	16	1.01 (0.58 to 1.65)	14	1.01 (0.55 to 1.69)	40.1	39.7	0.4 (−32.8 to 16.4)
Ovary	≤5	0.68 (0.22 to 1.60)	≤5	0.53 (0.11 to 1.56)	8.6	16.2	−7.6 (−69.6 to 3.1)
Prostate	65	1.18 (0.91 to 1.51)	56	1.07 (0.81 to 1.39)	202.4	189.1	13.2 (−47.5 to 56.8)
Testis	≤5	0.73 (0.09 to 2.63)	≤5	1.03 (0.12 to 3.70)	7.2	7.0	0.2 (−53.0 to 5.3)
Urinary bladder	11	0.71 (0.35 to 1.26)	10	0.76 (0.36 to 1.40)	16.0	21.0	−5.0 (−28.4 to 4.6)
Kidney and renal pelvis	11	0.86 (0.43 to 1.53)	11	0.95 (0.48 to 1.71)	17.6	18.5	−0.9 (−19.1 to 7.3)
Brain and other nervous system	7	1.23 (0.50 to 2.54)	≤5	0.96 (0.26 to 2.45)	6.4	6.7	−0.3 (−18.2 to 3.8)
Thyroid	16	1.15 (0.66 to 1.86)	16	1.15 (0.66 to 1.87)	25.6	22.2	3.3 (−13.2 to 11.9)
Hodgkin lymphoma	8	2.60 (1.12 to 5.13)	≤5	0.48 (0.01 to 2.66)	1.6	3.3	−1.7 (−158.3 to 1.0)
Non-Hodgkin lymphoma	13	0.76 (0.40 to 1.29)	20	1.40 (0.86 to 2.16)	32.0	22.8	9.1 (−5.2 to 17.2)
Multiple myeloma	≤5	0.76 (0.21 to 1.95)	≤5	1.09 (0.35 to 2.55)	8.0	7.3	0.7 (−14.8 to 4.9)
Leukemia	8	0.86 (0.37 to 1.69)	8	1.06 (0.46 to 2.09)	12.8	12.1	0.7 (−15.0 to 6.7)

Abbreviations: NYS, New York State; RD, rate difference.
[a] Analysis limited to the 32 740 participants not involved in rescue/recovery with known race/ethnicity.
[b] By the late period, of the 32 740 participants not involved in rescue/recovery with known race/ethnicity, 524 had been either diagnosed with cancer or died during the early period, and were therefore not eligible for inclusion in the late period analysis.
[c] Defined as the first primary cancers that were diagnosed between enrollment and December 31, 2006. All observed cancer cases were documented in the NYS cancer registry (n=366) and other state cancer registries (Connecticut=2, Florida=5, Massachusetts=2, New Jersey=3, and Pennsylvania=3). Exact numbers not provided to comply with internal New York City Department of Health and Mental Hygiene and New York State cancer registry policies of not reporting small numbers.
[d] Expected cancers are based on 2003-2006 NYS incidence rates for the early period and 2007-2008 rates for the later period.
[e] Defined as the first primary cancers that were diagnosed between January 1, 2007, and December 31, 2008. All observed cancer cases were documented in NYS cancer registry (n=308), and other state cancer registries (California=4, Connecticut=1, Florida=6, North Carolina=1, New Jersey=3, and Pennsylvania=1). Exact numbers not provided to comply with internal New York City Department of Health and Mental Hygiene and New York State cancer registry policies of not reporting small numbers.

Significant excess risks for prostate and thyroid cancers were observed. Both cancers are frequently detected during routine screening examinations,[22,23] and are potentially subject to surveillance bias. To address this bias, we compared the proportion having a routine physical checkup within the preceding 12 months between those with and without subsequent cancer. The proportions were nearly identical. Furthermore, the respective proportions of prostate and thyroid cancer that were stage I at diagnosis (85% and 66%) were similar to those of the NYS population.[24] These observations suggest that cancer cases in this study may not have received more thorough cancer screening than the NYS population in general, although they do not eliminate the possible role of surveillance bias altogether. Also, our findings might be prone to type I error given the large number of comparisons.

The etiologies of thyroid and prostate cancers are quite different. Thyroid cancer can be caused by ionizing radiation,[25] but potentially carcinogenic levels of radiation were neither documented nor suspected at the WTC site. Many occupational and environmental causes of prostate cancer have been suggested but studies have been largely inconsistent or inconclusive.[26] Hematological cancers are of special interest because they are generally regarded as having shorter latency periods than solid tumors[27] and are associated with radiation and certain chemicals,[28] and therefore could be early indicators of cancer risk. We observed 7 later period cases of multiple myeloma among rescue/recovery workers, yielding a significantly elevated SIR of 2.85. The age distribution of these 7 cases was consistent with that of the general population, in contrast to the much younger age distribution in a case series report.[29]

In the study by Zeig-Owens et al[11] of an FDNY cohort, the SIR was based on fewer than 5 cases of multiple myeloma and was not statistically significant. Multiple myeloma has been associated with a variety of occupations, including fire fighting,[30] painting, farming and other agricultural work,[31,32] as well as with exposure to benzene.[16] However, few specific environmental agents have been consistently linked to myeloma. None of the other hematological sites was associated with an elevated SIR among rescue/recovery workers. Reduced risk of later period lung cancer in the participants not involved in rescue/recovery was observed. Lung cancer with its typically long latency period will remain a concern given WTC exposure to asbestos, silica, and other carcinogens.[33]

This study has important strengths. It is the first WTC cancer incidence study that includes both sexes, all ages and races, and both rescue/recovery

Table 5. Cox Proportional Hazard Models to Assess Risk of Cancer as a Function of World Trade Center Exposure Level by Rescue/Recovery Work Status During the Entire Follow-up Period (2003-2008)[a]

	Rescue/Recovery Workers (n = 21 371)[b]			Participants Not Involved in Rescue or Recovery (n = 33 928)		
	No. With First Incident Cancer	Person-Years of Follow-up	Adjusted HR (95% CI)[c]	No. With First Incident Cancer	Person-Years of Follow-up	Adjusted HR (95% CI)[c]
Lung and bronchus						
Low exposure level	2	6873	1 [Reference]	24	76 259	1 [Reference]
Intermediate exposure level	22	76 867	1.4 (0.3-6.5)	41	67 423	1.2 (0.7-2.0)
High exposure level	2	13 395	1.0 (0.1-7.8)	3	11 848	0.6 (0.2-2.1)
Prostate						
Low exposure level	8	3582	1 [Reference]	62	35 460	1 [Reference]
Intermediate exposure level	88	62 576	0.8 (0.4-1.7)	57	28 464	0.9 (0.6-1.4)
High exposure level	14	12 349	0.8 (0.3-1.9)	10	4567	1.1 (0.6-2.2)
Thyroid						
Low exposure level	2	6873	1 [Reference]	19	76 259	1 [Reference]
Intermediate exposure level	17	76 867	0.7 (0.1-3.0)	10	67 423	0.5 (0.2-1.2)
High exposure level	7	13 395	1.3 (0.3-7.0)	2	11 848	0.6 (0.1-2.7)
Non-Hodgkin lymphoma						
Low exposure level	0	6873	NA	13	76 259	1 [Reference]
Intermediate exposure level	20	76 867	1 [Reference]	18	67 423	1.2 (0.6-2.4)
High exposure level	3	13 395	0.8 (0.2-2.8)	3	11 848	1.2 (0.3-4.4)
Hematological cancer[d]						
Low exposure level	1	6873	1 [Reference]	38	76 259	1 [Reference]
Intermediate exposure level	41	76 867	3.7 (0.5-27.6)	30	67 423	0.8 (0.5-1.3)
High exposure level	9	13 395	4.5 (0.5-37.4)	3	11 848	0.4 (0.1-1.5)

Abbreviations: HR, hazard ratio; NA, not applicable.
[a] Exposure level definitions appear in the eTable at http://www.jama.com.
[b] Excludes workers who worked exclusively on Staten Island site.
[c] Adjusted for age at enrollment, race/ethnicity, sex, income in 2002, education, source of enrollment, smoking status, and preexisting medical conditions at enrollment.
[d] Included leukemia, Hodgkin and non-Hodgkin lymphomas, and multiple myeloma.

workers and those not involved in rescue/recovery. In addition, we constructed a multilevel metric of WTC exposure to examine dose-response relationships. The analysis considered latency to the development of cancer by dividing the follow-up into early and later periods.

There are also important limitations. First, WTC exposures were self-reported 2 to 3 years after the September 11 attacks, and thus are subject to recall error. However, numerous registry studies have established strong associations between reported levels of exposures and specific health outcomes that display a high degree of internal consistency.[2,12] Second, the cancer cases identified through linkages with state cancer registries might be underestimated, especially among those without a social security number because about 23% of enrollees did not provide one. However, the percentage of enrollees having a full or partial social security number among cancer cases was similar to that in noncases. Third, because 70% of registry enrollees were self-identified,[13] there may be self-selection bias.[34] We attempted to mitigate this bias by restricting the analyses to individuals without prior invasive cancer history documented in any of the 11 state cancer registries and focusing on cancer incidence in the later period. Fourth, multiple comparisons (23 cancers for 2 periods) could produce statistically significant findings that are in fact due to chance. Fifth, the relatively small number of persons with cancer in both the low- and high-exposure categories, and the relatively short follow-up period limited our ability to detect excess cancer risk and the association with intensity of WTC exposure, particularly for rarer cancers. Future in-depth studies of rarer cancers may benefit from combining data across the September 11 survivor and/or responder cohorts to increase sample size. In addition, we lacked information on cancer risk factors, eg, family cancer history, occupational exposures before or after September 11, history of exposure to other environmental carcinogens, and medical screening history, especially for prostate cancer.

CONCLUSION

In summary, this study found significantly increased prostate and thyroid cancers and multiple myeloma among rescue/recovery workers in the later period that were not significantly associated with intensity of WTC exposures. Given the relatively short follow-up time and lack of data on medical screening and other risk factors, the increase in prostate and thyroid cancers and multiple myeloma should be interpreted with caution. The etiological role of WTC exposures in these 3 cancers is unclear. Longer follow-up of rescue/recovery workers and participants not involved in rescue/recovery is needed with attention to selected cancer sites and to examine risk for cancers with typically long latency periods.

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Study concept and design: Li, Cone, Brackbill, Farfel, Greene, Stayner, Stellman.
Acquisition of data: Li, Cone, Brackbill, Stellman.
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Whatever affects one directly affects all indirectly. I can never be what I ought to be until you are what you ought to be, and you can never be what you ought to be until I am what I ought to be. This is the interrelated structure of reality.

—Martin Luther King (1929-1968)

