Early assessment of cancer outcomes in New York City firefighters after the 9/11 attacks: an observational cohort study

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Summary

Background The attacks on the World Trade Center (WTC) on Sept 11, 2001 (9/11) created the potential for occupational exposure to known and suspected carcinogens. We examined cancer incidence and its potential association with exposure in the first 7 years after 9/11 in firefighters with health information before 9/11 and minimal loss to follow-up.

Methods We assessed 9853 men who were employed as firefighters on Jan 1, 1996. On and after 9/11, person-time for 8927 firefighters was classified as WTC-exposed; all person-time before 9/11, and person-time after 9/11 for 926 non-WTC-exposed firefighters, was classified as non-WTC exposed. Cancer cases were confirmed by matches with state tumour registries or through appropriate documentation. We estimated the ratio of incidence rates in WTC-exposed firefighters to non-exposed firefighters, adjusted for age, race and ethnic origin, and secular trends, with the US National Cancer Institute Surveillance Epidemiology and End Results (SEER) reference population. CIs were estimated with overdispersed Poisson models. Additional analyses included corrections for potential surveillance bias and modified cohort inclusion criteria.

Findings Compared with the general male population in the USA with a similar demographic mix, the standardised incidence ratios (SIRs) of the cancer incidence in WTC-exposed firefighters was 1·10 (95% CI 0·98–1·25). When compared with non-exposed firefighters, the SIR of cancer incidence in WTC-exposed firefighters was 1·19 (95% CI 0·96–1·47) corrected for possible surveillance bias and 1·32 (1·07–1·62) without correction for surveillance bias. Secondary analyses showed similar effect sizes.

Interpretation We reported a modest excess of cancer cases in the WTC-exposed cohort. We remain cautious in our interpretation of this finding because the time since 9/11 is short for cancer outcomes, and the reported excess of cancers is not limited to specific organ types. As in any observational study, we cannot rule out the possibility that effects in the exposed group might be due to unidentified confounders. Continued follow-up will be important and should include cancer screening and prevention strategies.

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Introduction

The attacks on the World Trade Center (WTC) on Sept 11, 2001 (9/11), created an environmental disaster of unprecedented scale for the New York area, and the potential for occupational exposure to known and suspected carcinogens. Many first responders, including about 12 500 firefighters employed by the Fire Department of the City of New York (FDNY), were exposed to aerosolised dust—an amalgam of pulverised cement, glass fibres, asbestos, lead, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, and polychlorinated furans and dioxins produced as combustion byproducts from the collapsed and burning buildings.[1] They were also exposed to toxic fumes, initially from burning jet fuel and over the subsequent 10-month recovery effort from diesel fuel from heavy equipment.

The full extent of the association between WTC-exposure and cancer occurrence remains unknown. So far, only one study investigating WTC-related cancer has described eight cases of multiple myeloma in WTC responders, but uncertainty related to the definition of exposure and the exact population at risk limit the generalisability of its conclusions.[2] Our study is a preliminary effort to examine incidence of cancers occurring within the first 7 years after 9/11 in a cohort of nearly 10 000 male firefighters with known health information before 9/11 and minimal loss to follow-up.

Methods

Study population

The original study population consisted of 10 567 firefighters who were employed by FDNY for at least 18 months, were active firefighters on Jan 1, 1996, and if alive on Sept 12, 2001, also had known WTC-exposure status (WTC-exposed or non-exposed). The Jan 1, 1996, start date was chosen on the basis of completeness of the New York state tumour registry data. We excluded data from 576 firefighters who were or would have been aged

60 years or older on 9/11, because their small number could have generated statistically unstable age-adjusted rates. For the same reasons, we excluded data from 32 women, 13 Asians, and 8 Native Americans. Finally, we excluded 85 individuals who had a cancer diagnosis before 1996, resulting in a final analytic cohort of 9853 non-Hispanic white, non-Hispanic black, and Hispanic male firefighters. We received approvals from the institutional review boards of Montefiore Medical Center (Bronx, NY) and the New York State Department of Health. Additionally, because some firefighters moved outside of New York since retiring, we obtained institutional review board approvals from the Florida, Pennsylvania, North Carolina, and Virginia State Departments of Health. All institutional review boards approved participation on the basis of scientific merit and risk–benefit ratio, waiving informed consent.

Procedures

Data for race and ethnic origin, sex, years of service, dates of birth, FDNY employment status, and death were obtained from the FDNY employee database. Additional dates of death were obtained by linkage to the social security death index. Since 1980, the FDNY Bureau of Health Services has done mandatory health assessments of active firefighters every 18 months; this service was offered to retirees after 9/11. These visits include a physical examination, and since October, 2001, self-administration of comprehensive health questionnaires.

8560 of 9853 firefighters in the analytic cohort directly participated in FDNY health monitoring examinations after 9/11, reporting WTC-exposure status on their first questionnaire after 9/11. Of the remaining participants, we obtained exposure information either by phone or mail for 959 (10%) who had retired and were mostly living out of state (and did not return for monitoring). Additionally, 77 (1%) who died before 9/11 were classified as non-exposed because they did not have the opportunity to be exposed to the WTC site. 257 (3%) who died on 9/11 were classified as exposed because we know that they died at the WTC site on 9/11.

Firefighters were classified as WTC-exposed if they reported working at the WTC site for at least 1 day on any day before the site closed (July 25, 2002). Exposure categories are shown in table 1, which includes both the FDNY exposure categories (based on initial WTC arrival time)[3] and the common-exposure categories (types of WTC exposure on 9/11), as agreed by investigators from the four New York City cohorts of WTC-responders and rescue workers.[4] The FDNY categories start with the most exposed group, those arriving during the morning of 9/11 and end with the least exposed, those arriving any day between Sept 25, 2001, and July 25, 2002. The common-exposure categories describe three types of exposure on 9/11 and a level of exposure for those not present then but were present before the site closure. We obtained information about smoking status from the health questionnaires, which was divided into two categories: smokers were defined as ever-smokers (ie, current or former smokers) and those who never smoked were defined as never-smokers (ie, consistently never smokers).

	Number of WTC-exposed firefighters (N=8927*)
FDNY exposure categories†—time of first arrival at WTC site	
Morning of 9/11	1600 (18%)
Afternoon of 9/11	4409 (49%)
Day of Sept 12, 2001	1616 (18%)
Any day between Sept 13, 2001, and Sept 24, 2001	1211 (14%)
Any day between Sept 25, 2001 and July 25, 2002	91 (1%)
Common exposure categories‡—type of exposure on day of 9/11	
Heavily exposed to the dust cloud	1702 (19%)
Working on the pile but not heavily exposed to dust cloud	4218 (47%)
Present but not working on the pile and not heavily exposed to the dust cloud	123 (1%)
Not present in lower Manhattan on 9/11	2700 (30%)
Missing type of exposure information	184 (2%)

Data are number (%). The two exposure categories describe different types of exposure and therefore frequencies between them should not be compared. FDNY exposure categories define exposure as time of first arrival to work at WTC site. The common exposure categories do not require that individuals work at the WTC site but only their presence at the site. This definition accounts for the difference between 2918 exposed firefighters after Sept 11, 2001, in the FDNY exposure categories and 2700 in the common exposure categories. WTC=World Trade Center. FDNY=Fire Department of the City of New York. 9/11=Sept 11, 2001. *926 persons were never exposed to WTC site. †Expanded FDNY definition of WTC exposure.[3] ‡WTC-common-exposure definition.[4]

Table 1: **Distribution of exposure categories in World-Trade-Center-exposed firefighters**

Active FDNY firefighters are required to live in New York City or in nearby Westchester, Rockland, Orange, Nassau, or Suffolk New York state counties; after retirement, some move out of the New York State. We matched all individuals to state tumour registries in New York, Florida, Pennsylvania, North Carolina, and Virginia, where 4864 (93%) current WTC-exposed retirees and 758 (90%) current non-exposed retirees live. We generated a file of all FDNY firefighters including social security numbers (available for all firefighters), first, middle, and last names, race and ethnic origin, and birth date and received a linked file containing tumours of all behaviour codes (ie, invasiveness), date of diagnosis, laterality, staging, and the last date of complete data for those in our cohort. New York state tumour registry data are 97% or more complete from Jan 1, 1996.[5]

All primary malignant cancer cases reported to the FDNY Bureau of Health Services by questionnaire or reported in Bureau of Health Services medical assessments or records were reviewed by a trained clinician (NJ) who contacted participants and requested medical records. Additionally, we contacted 373 individuals in the analytic cohort who were alive at the end of the study, lived in a state where we did not have a tumour registry match, and had not returned for a monitoring examination to give them the opportunity to self-report a cancer diagnosis. We received responses from 188 (50%) individuals. Cancer reports from those contacted by mail or phone were similarly confirmed. Analyses included only confirmed cases for which we required a pathology report, or detailed notes or assessments from the treating physician (operative reports, oncology notes with diagnosis or treatment, formal consultations from related specialists, or physical findings consistent with oncological treatments or modalities).

We used confirmed cases, both self-reported with appropriate documentation and those obtained from any state tumour registry match, counting cases received from both sources only once. State tumour registry diagnoses were classified according to the International Classification of Diseases for Oncology (ICD-O-3).[6] Malignant cancer cases (ICD-O-3 behaviour 3) were included. Comparison rates generated from the US National Cancer Institute Surveillance Epidemiology and End Results (SEER) database included in-situ bladder cancers and excluded cutaneous basal-cell and squamous-cell cancers from cancer rates. We therefore used these criteria for consistency. Further information on WTC-case definitions has been reported.[7] The latest US national cancer rates from the SEER-13 registries database are available up to Dec 31, 2008, and were used to control for secular trends (changes in cancer incidence over time in the general US population).[8]

Since FDNY firefighters have full access to health care, with free care for established WTC-related disorders (which currently excludes cancers), we used a number of procedures to assess possible surveillance bias. First, we examined the stage at diagnosis for all cancer sites in WTC-exposed and non-exposed firefighters, and for common cancers, by individual cancer type (prostate, thyroid, non-Hodgkin lymphoma). Second, we examined the FDNY medical protocol to determine if any tests or procedures changed during the study period. The only change in FDNY medical protocol occurred in the year after 9/11 when surveillance chest CT scans were offered to high-risk firefighters (those with earliest arrival to the WTC site during the morning of 9/11 and current smokers). Records of 15 firefighters who had surveillance chest CT scans through FDNY 6 months or less before a cancer diagnosis (lung, liver, thyroid, non-Hodgkin lymphoma, and kidney) were identified for possible surveillance bias. We also identified prostate and haematological cancers diagnosed within 6 months of routine blood tests for possible surveillance bias, done as part of the FDNY Bureau of Health Services medical monitoring examinations, even though this protocol did not change during follow-up. Although there is no way to know for certain, these additional tests and screenings could have resulted in an earlier diagnosis of cancer. To account for this, we did additional analyses in which we delayed the diagnosis date by 2 years for these identified cancers, which were detected during either chest CT scans or routine FDNY blood tests, and compared the results with those obtained using the actual diagnosis dates. The 2-year delay in the diagnosis date was based on prior research.[9] Melanoma and colon cancer corrections were not made because no cases were diagnosed during FDNY monitoring examinations. These examinations did not include faecal-occult-blood testing or internal examinations (digital, sigmoidoscopy, or colonoscopy).

	Cohort (n=9853)
Race and ethnic origin	
Non-Hispanic white	9289 (94%)
Non-Hispanic black	294 (3%)
Hispanic	270 (3%)
Self-reported never smokers by end of study (n=8467)	5313 (63%)
Retired as of 9/11	1482 (15%)
Mean age as of 9/11 (years)	44·0 (6·7)
Mean age at start of follow-up (years)	38·4 (6·7)
Mean years of service as FDNY firefighters	20·8 (5·9)
Mean length of follow-up (years)	12·7 (1·2)

Data are number (%) or mean (SD). 9/11=Sept 11, 2001. FDNY=Fire Department of the City of New York.

Table 2: **Selected characteristics of the total Fire Department of the City of New York analytic cohort**

Statistical analyses

For active firefighters or those who retired within New York State, Florida, Pennsylvania, North Carolina, or Virginia, follow-up time began on Jan 1, 1996, and ended on the earliest date of the following events: death, first cancer diagnosis, or at the end of the study (Dec 31, 2008). If an individual retired to a state where we did not have data from a registry match, follow-up ended on the earliest date of the following events: death, first cancer diagnosis, the most recent FDNY Bureau of Health Services examination, or if no post-retirement examination date, their FDNY retirement date, or at the end of study.

WTC exposure was modelled as a time dependent variable: all firefighter person-time was classified as non-exposed before 9/11. After 9/11, exposed firefighter person-time was classified as exposed, and the non-exposed firefighter person-time continued to be classified as non-exposed. Since those who died before 9/11 did not have an opportunity to become exposed, they only contribute non-exposed person-time. The 257 firefighters who died on 9/11 were classified as exposed for 1 day, contributing a combined person-time of less than 1 year (0·001% of the total person-years) to the overall exposed person-time.

We estimated expected numbers of all cancer sites, and standardised incidence ratios (SIRs) for all cancer sites combined and for site-specific cancer types, with the SEER reference population rates. The SEER rates are calculated separately by 5-year age bands, race and ethnic origin, and calendar year. Each individual was given an expected number of incident cancers according to his age and race and ethnic origin at each year of follow-up in the WTC-exposed and non-exposed groups. These individual expected numbers were summed to produce the reported expected numbers. The obtained SIR is the number of observed incident cancers divided by the expected number of cancers from SEER. We calculated WTC-exposed and non-exposed SIRs to assess differences in cancer rates between these two groups. To test for an exposure gradient, SIRs were calculated by comparing each exposure category with the non-exposed category.

Our primary outcome measure was the risk ratio for all cancers and site-specific cancers adjusted for age, race and ethnic origin, and secular trends in incidence over time, with SEER, which is calculated as the ratio of the exposed to non-exposed SIRs. 95% CIs for the SIRs (and their risk ratios) were conservatively estimated with overdispersed Poisson models; these models were fit without and with correction for surveillance bias (corrected SIR). We assessed effect modification (by employment status [active or retired] and smoking status) by testing interaction variables. We calculated risk ratios for ever-smokers and never-smokers. Smoking information was randomly imputed for 1409 individuals missing smoking status. This imputation was done with a multiple imputation approach that randomly assigned 888 of those missing smoking status to be never-smokers and 521 to be ever-smokers to match the cohort rate of 63% never-smokers in those with known smoking status. We did ten imputations to obtain our final rate ratios for ever-smokers and never-smokers.[10]

Various additional secondary analyses were done. We recalculated SIR ratios after lagging the diagnosis dates of all cancers potentially detected by FDNY surveillance (n=25) to dates beyond the study period. We controlled for possible latency in cancer incidence in WTC-exposed firefighters by dividing the follow-up period into early (9/11 to Dec 31, 2004) and late (Jan 1, 2005, to Dec 31, 2008) periods. We also fit Cox survival models, with age as the timescale, adjusting for race and ethnic origin, and compared the hazard ratio of WTC-exposed to non-exposed firefighters to the SIR from the primary analysis. Cox models provided a more accurate adjustment for age than did our primary analysis, but did not adjust for secular trends with SEER comparison rates. We also modified the inclusion criteria of the primary cohort and calculated SIRs and 95% CIs with the overdispersed Poisson models described above. The first modified cohort, the multiple-primary-cancers cohort (n=9936), included all primary cancers and no longer excluded individuals who had a cancer diagnosis before 1996. The expanded cohort (n=10 505) included

	Observed	Expected	SIR (95% CI)
All sites			
Exposed (61 884 person-years)	263	238	1·10 (0·98–1·25)
Non-exposed (60 761 person-years)	135	161	0·84 (0·71–0·99)
SIR ratio*	··	··	1·32 (1·07–1·62)
All sites (corrected)†			
Exposed	242	238	1·02 (0·90–1·15)
Non-exposed	135	161	0·84 (0·71–0·99)
SIR ratio*	··	··	1·21 (0·98–1·49)
Oesophagus			
Exposed	≤5	3	0·58 (0·15–2·32)
Non-exposed	≤5	2	0·44 (0·06–3·13)
SIR ratio*	··	··	1·32 (0·12–14·53)
Stomach (including gastro-oesophageal junction)			
Exposed	8	4	2·24 (0·98–5·25)
Non-exposed	≤5	2	1·23 (0·40–3·83)
SIR ratio*	··	··	1·82 (0·44–7·49)
Colon (excluding rectum)			
Exposed	21	14	1·52 (0·99–2·33)
Non-exposed	9	9	1·01 (0·53–1·94)
SIR ratio*	··	··	1·50 (0·69–3·27)
Pancreas			
Exposed	≤5	5	0·78 (0·29–2·09)
Non-exposed	≤5	3	0·31 (0·04–2·20)
SIR ratio*	··	··	2·52 (0·28–22·59)
Lung			
Exposed	9	21	0·42 (0·20–0·86)
Non-exposed	8	15	0·52 (0·26–1·05)
SIR ratio*	··	··	0·80 (0·29–2·18)
Lung (corrected)†			
Exposed	6	21	0·28 (0·13–0·62)
Non-exposed	8	15	0·52 (0·26–1·05)
SIR ratio*	··	··	0·53 (0·18–1·54)
Melanoma			
Exposed	33	21	1·54 (1·08–2·18)
Non-exposed	15	16	0·95 (0·57–1·58)
SIR ratio*	··	··	1·61 (0·87–2·99)
Prostate			
Exposed	90	60	1·49 (1·20–1·85)
Non-exposed	45	33	1·35 (1·01–1·81)
SIR ratio*	··	··	1·11 (0·77–1·59)
Prostate (corrected)†			
Exposed	73	60	1·21 (0·96–1·52)
Non-exposed	45	33	1·35 (1·01–1·81)
SIR ratio*	··	··	0·90 (0·62–1·30)
Testicular			
Exposed	≤5	6	0·86 (0·36–2·06)
Non-exposed	11	7	1·54 (0·85–2·78)
SIR ratio*	··	··	0·56 (0·19–1·60)
Bladder			
Exposed	11	11	1·01 (0·56–1·83)
Non-exposed	6	8	0·79 (0·36–1·76)
SIR ratio*	··	··	1·28 (0·47–3·46)

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	Observed	Expected	SIR (95% CI)
(Continued from previous page)			
Kidney			
Exposed	10	12	0·86 (0·46–1·60)
Non-exposed	≤5	7	0·30 (0·07–1·18)
SIR ratio*	..	..	2·91 (0·64–13·30)
Thyroid			
Exposed	17	6	3·07 (1·86–5·08)
Non-exposed	≤5	3	0·59 (0·15–2·36)
SIR ratio*	..	..	5·21 (1·19–22·74)
Thyroid (corrected)†			
Exposed	12	6	2·17 (1·23–3·82)
Non-exposed	≤5	3	0·59 (0·15–2·36)
SIR ratio*	..	..	3·67 (0·82–16·42)
Hodgkin's lymphoma			
Exposed	0	2	..
Non-exposed	≤5	2	0·82 (0·20–3·27)
SIR ratio*	..	..	..
Non-Hodgkin lymphoma			
Exposed	21	13	1·58 (1·03–2·42)
Non-exposed	9	11	0·83 (0·43–1·60)
SIR ratio*	..	..	1·90 (0·87–4·15)
Non-Hodgkin lymphoma (corrected)†			
Exposed	20	13	1·50 (0·97–2·33)
Non-exposed	9	11	0·83 (0·43–1·60)
SIR ratio*	..	..	1·81 (0·82–3·97)
Multiple myeloma			
Exposed	≤5	3	1·49 (0·56–3·97)
Non-exposed	0	2	..
SIR ratio*	..	..	..
Leukaemia			
Exposed	9	6	1·40 (0·73–2·70)
Non-exposed	7	5	1·47 (0·63–3·40)
SIR ratio*	..	..	0·98 (0·33–2·77)

Standardised incidence ratios (SIRs) are ratios of observed to expected cancers established by the cancer incidence in the reference USA (Surveillance Epidemiology and End Results) population, standardised to match the age and race and ethnic origin demographics of the Fire Department of the City of New York firefighter cohort. SIR ratios are the ratios of the World-Trade-Center (WTC) exposed SIRs to the non-exposed SIRs. SIR=standardised incidence ratios. *Exposed *vs* non-exposed. †Corrected for surveillance bias by lagging the diagnosis date by 2 years for 25 cases. All person-time before Sept 11, 2001 (9/11), was classified as non-WTC-exposed. On and after 9/11, person-time for 8927 persons was classified as WTC-exposed, while person-time for 926 remained non-exposed. We did not include sites with too few cancers for our analysis and therefore the sum of site-specific cancers in this table does not include all observed cases.

Table 3: **Observed and expected number of cancers and standardised incidence ratios (SIRs and corrected SIRs) for male firefighters from the Fire Department of the City of New York with USA (Surveillance Epidemiology and End Results) cancer rates for comparison**

firefighters who began employment between Jan 1, 1996, and Sept 10, 2001. All analyses were done with SAS (version 9.2). SEER comparison rates were generated with SEER*Stat (version 7.0.4).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Table 2 shows selected characteristics of the primary analytic cohort. The mean age at first cancer diagnosis was older in the WTC-exposed group (52·5 [SD 6·4] years) than in the non-exposed group (49·9 [SD 8·9] years).

We identified a modest effect of WTC exposure for all cancers combined by comparing the ratios in the exposed group to those in the non-exposed group (table 3). An exposure-response gradient generated with the FDNY exposure categories[3] or the common-exposure categories[4] was not significant. We did not identify any evidence of effect modification by employment status (active or retired), and therefore, did not include this interaction term in the model. In analyses of all cancer sites by smoking status, the rate ratio for ever-smokers was 1·50 (95% CI 0·72–2·28) and for never-smokers 1·20 (0·54–1·85). All nine lung cancers in exposed firefighters occurred in smokers.

Site-specific cancer SIR ratios (exposed *vs* non-exposed) were not significantly increased, although we noted a trend towards an increase in ten of 15 sites. We noted, however, significantly lower rates of lung cancer in WTC exposed participants (SIR 0·42, 95% CI 0·20–0·86) than in the general population.

To correct for possible surveillance or lead-time bias, we lagged the diagnosis date by 2 years for 25 cases, effectively eliminating 21 from the analysis of the WTC-exposed group. We reported only a modest reduction in the SIR ratio (exposed *vs* non-exposed) for all cancer sites from 1·32 (95% CI 1·07–1·62) without correction to 1·21 (0·98–1·49) with correction. Further lagging of the diagnosis dates to eliminate all 25 cases, because they occurred after the close of the study, reduced the SIR ratio to 1·19 (0·96–1·47; figure). Surveillance bias was also assessed by comparing the stage at diagnosis for cancer with known stage matched from the New York State tumour registry (n=338) by exposure status. We identified no significant differences in the proportion of different cancer stages at diagnosis by exposure status: 152 (67%) localised, 39 (17%) regional, and 35 (16%) distant in WTC-exposed firefighters and 70 (63%) localised, 20 (18%) regional, and 22 (20%) distant in non-exposed firefighters (p=0·59).

The figure shows the all cancer-site results of the primary and secondary analyses, all of which show similar modest increases in cancer rates for WTC-exposed firefighters compared with non-exposed firefighters; it also includes an analysis controlling for possible latency by dividing the follow-up period into early (9/11 to Dec 31, 2004) and late (Jan 1, 2005, to Dec 31, 2008) periods. The SIR was 1·28 (95% CI 0·99–1·67) for all cancer sites in the WTC-exposed group occurring in the early period compared with cancers in the non-exposed group, from Jan 1, 1996, to

Dec 31, 2008. The SIR was 1·34 (95% CI 1·07–1·67) for all cancer sites in the exposed group occurring in the late period compared with all cancer sites in the non-exposed group, from Jan 1, 1996, to Dec 31, 2008.

Discussion

WTC-exposed firefighters had about 10% higher overall cancer incidence ratios than those expected in a similar demographic mix from the general male population in the USA and about 32% higher than in non-exposed firefighters (panel). We identified these differences in our primary analysis in which we compared only first cancers in the FDNY cohort with all tumours reported in SEER reference rates. Additional analyses consistently showed similar modest increases in all cancer sites combined for WTC-exposed firefighters compared with non-exposed firefighters. There was limited power to characterise cancer site-specific rate ratios or an exposure response gradient on the basis of either FDNY arrival time or the common WTC-exposure categories.

Firefighting might be associated with increased cancer rates, but previous work has not revealed clear and reproducible cancer-site-specific risks across studies.[11–14] Although we do not know the number of fires each firefighter was exposed to, we believe the observed relative excess in cancer cases in WTC-exposed firefighters was unlikely to be the result of non-WTC firefighting exposures, because since 9/11, structural fires have decreased,[15–17] personal protective equipment (required since the 1970s) has improved,[18] self-contained breathing equipment use has increased (mandatory since the 1980s), and smoking rates in firefighters have declined.[19] Milham[20] has suggested that cancer in firefighters is associated with radio frequency radiation rather than other exposure pathways such as inhalation; we were unable to assess this hypothesis in our current cohort.

Comparison of WTC-exposed firefighters and non-exposed firefighters with the general population with SEER rates allowed us to account for secular trends in cancer incidence over time. We noted similar or lower than expected cancer rates in the non-exposed firefighters compared with SEER rates, which we attribute to a healthy worker effect: FDNY firefighters have lower smoking rates, stringent pre-employment health requirements, and greater physical fitness standards than the general population.[21] This effect is specifically seen in the low rates of lung cancer reported in our study. The possibility that firefighters might have a different background cancer risk than the general population, as shown by comparison with SEER reference rates, argues strongly in favour for the use of the ratio of SIRs, rather than the SIR alone, as we did in our primary analysis. Non-exposed firefighters can be expected to be similar to exposed firefighters in relation to unidentified potential confounders, although we cannot rule out residual confounding as a cause of observed effects.

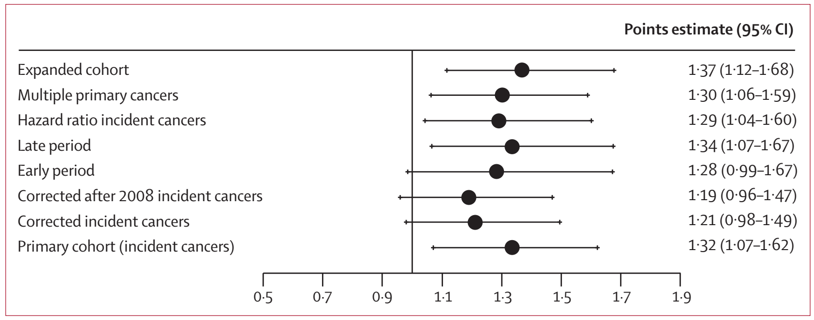

***Figure:* Primary and secondary analyses displaying point estimates and 95% CIs for all cancer sites combined**
Primary cohort (corrected after 2008 incident cancers): standardised incidence ratios (SIRs) ratio of first cancers in World Trade Center (WTC) exposed firefighters versus non-exposed firefighters. Corrected incident cancers: SIR ratio of first cancers in exposed versus non-exposed firefighters, with the diagnosis date delayed by 2 years for 25 cases, which might have been detected by FDNY screening. Corrected after 2008 incident cancers: SIR ratio of first cancers in exposed versus non-exposed firefighters with diagnosis dates delayed to beyond 2008, the study period, for 25 cases that might have been detected by FDNY screening. Early period: SIR ratio of exposed firefighters in the early follow-up period (Sept 11, 2001 [9/11], to Dec 31, 2004) after 9/11, versus non-exposed firefighters. Late period: SIR ratio of exposed firefighters in the late follow-up period (Jan 1, 2005, to Dec, 31, 2008) after 9/11 versus non-exposed firefighters. Hazard ratio incident cases: ratio of hazard-ratio rates of first cancers in exposed firefighters versus non-exposed firefighters estimated with the Cox model. Multiple primary cancers: SIR ratio of multiple primary cancers in exposed firefighters versus non-exposed firefighters. Expanded cohort: SIR ratio of first cancers in exposed firefighters versus non-exposed firefighters including those who began employment between Jan 1, 1996, and Sept 10, 2001.

We made great efforts to address lead time and surveillance bias. Since 1996, firefighters have routinely received physical examinations, which include prostate-specific antigen screening, other routine blood work, and chest radiographs. After 9/11, firefighters have also had access to free health care for WTC-related health disorders including surveillance chest CT scans for high-risk firefighters. We corrected our analyses for possible lead time or surveillance bias by delaying the recorded date of diagnosis by 2 years or more. We showed that SIRs for the WTC-exposed firefighters remained increased, as was the case when we limited cancers in the exposed firefighters to those occurring during or after 2005, to allow for a latency period. We point out, however, that our correction for cancer screening could only be applied to examinations done during an FDNY medical monitoring programme visit; we were unable to correct for possible surveillance bias in screenings that occurred outside of FDNY in either the exposed or non-exposed firefighters, both of which have greater cancer concerns and more liberal health insurance than do the general population.

We examined the distribution of cancer by stage, because aggressive case ascertainment might be expected to result in the detection of early stage tumours, but we failed to see an increase in the proportion of cancers that were classified as local versus regional or distant for any cancer site. This lack of difference might have been caused by a secular trend toward diagnoses of high severity, but we have seen no evidence of this trend nationally.[22] Furthermore, the mean age at diagnosis of cancers in the WTC-exposed group was 2·6 years older than that in the non-exposed group, also arguing against lead time bias. Therefore, although we cannot rule out

Panel: Research in context

Systematic review

We searched PubMed from September, 2001, to April, 2011, using keywords "cancer" and "world trade center" for reports investigating cancer incidence in World-Trade-Center (WTC) exposed cohorts. No cohort studies were identified. The only cancer study to date is a case series in which uncertainty about the exact population at risk limits generalisability to other WTC-exposed populations.

Interpretation

Our findings support continued monitoring of firefighters and other WTC-exposed cohorts to fully assess cancer risk related to these unique exposures.

the possibility that surveillance or lead-time bias accounts for some portion of the recorded increase in WTC-exposed firefighters, we noted that after correction, SIRs for all cancer sites were increased from 19% to 21% in the exposed group, arguing against considerable bias.

We did not limit analyses to cancers thought to have short latency periods, such as haemopoietic cancers, because we identified few epidemiological data from general populations on the latency between short-term, high-intensity exposure and cancer incidence other than for radiation and infectious agents.

An association between WTC exposure and cancer is biologically plausible, because some contaminants in the WTC dust, such as polycyclic aromatic hydrocarbons, polychlorinated biphenyls, and dioxins, are known carcinogens.[1,23–25] Although some contaminants could cause cancer directly, WTC exposure could also trigger chronic inflammation, through microbial infections, autoimmune diseases, or other inflammatory disorders, all of which have been reported as factors in oncogenesis, both experimentally and epidemiologically.[26–31] The prevalence of specific cancers (ie, prostate, thyroid, melanoma, non-Hodgkin lymphoma) associated with inflammation[32,33] was also increased in our analysis. Many disorders occurring after 9/11 including asthma, bronchitis, sinusitis, and acid reflux, which have been reported as highly prevalent in our cohort[5,34] and other WTC cohorts,[35,36] have been associated with chronic inflammation. Such inflammation could lead to cancer because of the activities of leucocytes, including the production of proteins (cytokines and chemokines) that alter the behaviour of target cells, stimulation of blood vessel growth (angiogenesis), and tissue remodelling. Immune cells also produce oxygen radicals that can cause DNA mutations.[37] The relation between inflammation and cancer, and the time interval for such an effect, however, is not well understood and requires additional research.

By comparing cancer SIRs in WTC-exposed firefighters with incidence ratios in non-exposed firefighters, our analyses document a modest excess of cancer cases in exposed firefighters, reducing the healthy worker effect for cancer that we identified in non-exposed firefighters. This excess of cancer cases remained after correction for possible surveillance bias and after classification of cancers occurring only in 2005 or later as potentially related to WTC-exposure. We remain cautious in our interpretation of these findings because the time interval since 9/11 is short for cancer outcomes, the recorded excess of cancers is not limited to specific sites, and the biological plausibility of chronic inflammation as a possible mediator between WTC-exposure and cancer outcomes remains speculative.

Furthermore, we caution against generalising our findings to other WTC worker or resident cohorts, because firefighters experienced uniquely intense WTC exposures. Although, as in any observational study, to rule out the effect of surveillance bias or potential unmeasured confounders is impossible, we have gone to great lengths to assess and correct for known and potential biases. Continued follow-up of this cohort and other WTC-exposed cohorts is crucial and should include cancer screening and prevention strategies.

Conflicts of interest

We declare that we have no conflicts of interest.

Contributors

OD, NJ, DP, KK, and RZ-O assisted in clinical case confirmation. NJ and RZ-O managed the databases. CH, TS, and RZ-O analysed the data. DP and MW oversaw the research and preparation of the report. HC, CH, DP, TR, TS, JW, MW, and RZ-O contributed to the methodology and study design. MW, RZ-O, TS, CH, DP drafted the report, which was edited by TA, HC, OD, NJ, KK, TR, and JW.

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