

## Supplementary Online Content

Singh A, Zeig-Owens R, Moir W, et al. Estimation of future cancer burden among rescue and recovery workers exposed to the World Trade Center disaster. *JAMA Oncol*. Published online April 26, 2018. doi:10.1001/jamaoncol.2018.0504

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### eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

## eMethods

### Study Population

The FDNY-WTCHP includes 15,507 active and retired firefighters and emergency medical service workers. Individuals were considered to be WTC-exposed, and therefore eligible for inclusion in the study cohort, if they were involved in the rescue/recovery effort at the WTC site any time between September 11, 2001 (9/11), and the date of site closure (July 25, 2002). Data from individuals who before 2012 either developed cancer (n=901) or were cancer-free but died (n=132) were used to determine pre-2012 cancer counts and cohort incidence rates. These 1,033 individuals were excluded from the final study population, which was limited to the at-risk population of 14,474 FDNY-WTCHP participants who were alive and free of cancer as of the beginning of 2012, the first year for which we did not have complete cancer data.

### Baseline Characteristics

We assessed participants' race/ethnicity, sex, and age in each year of the study period, as estimation of future cancer cases in the FDNY-WTCHP cohort required the use of recent race-, sex- and age-specific cancer incidence rates. FDNY employees self-report race/ethnicity to FDNY Human Resources, and so we obtained this information from the FDNY Human Resources database, in addition to information on participants' sex and dates of birth.

### FDNY Medical Monitoring

Both actively employed and retired WTC-exposed FDNY rescue and recovery workers undergo annual medical monitoring examinations at the FDNY Bureau of Health Services; these involve a pulmonary function test, a complete blood count, chest CT scan (every other year), examination by a physician, and completion of health questionnaires. Information about participants' WTC exposure, or their initial arrival time at the WTC site, was taken from each individual's first post-9/11 monitoring questionnaire.

### Regional (NYC) Cancer Rates

We obtained age-, race- and sex-specific cancer rates from the New York State Cancer Registry (NYSCR). Selecting 2007-2011 NYSCR data for the New York City region, we extracted incidence rates for the most common site-specific cancers in the WTC-exposed cohort, and for all cancers combined. Age-specific rates were grouped in the 5-year bands shown in eTable 1.

### FDNY-WTCHP Cancer Rates

Cancer diagnoses that occurred in our cohort before 1/1/2012 were confirmed either by matching to state cancer registries or by a trained clinician's (NJ) review of medical records. Since over 85% of individuals enrolled

in the FDNY-WTCHP are white males, we were able to calculate stable, age-specific cohort cancer rates only for this subgroup. A cancer diagnosis that occurred between 1/1/2007 and 12/31/2011 in the white male subgroup was considered an incident case of a site-specific cancer if it was the first instance of a malignant tumor at that site. When determining the number of cancers at all sites, a diagnosis was added to the total case count if it was the first tumor of any cancer subtype (including bladder in-situ) recorded for an individual. Nonmalignant tumors and skin carcinomas (basal or squamous cell) were excluded from this case definition. The calculated cancer rates were used in an analysis in which we compared the future incidence estimates that resulted from using these rates to estimates produced by NYC rates for the white male subgroup (N=12,374).

Cases of prostate, lung, bladder, kidney, thyroid, and the hematologic cancers (Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, multiple myeloma, and other hematopoietic cancers) may be detected earlier in the FDNY-WTCHP cohort than they would be in a general population, due to the routine screening procedures (blood tests, chest CT scans) that are part of FDNY medical monitoring. In order to create a second set of FDNY-WTCHP rates that were adjusted for potential surveillance bias, we identified pre-2012 cases of the above-mentioned cancers that were diagnosed less than six months after routine monitoring (N=118) and delayed the diagnosis dates of these cases by two years. A two-year lag in diagnosis date was used because previous research showed that two years was the average screening lead time for prostate cancer diagnosis.<sup>1</sup> We then recalculated the 2007-2011 rates of the aforementioned cancer types and of all cancers combined in white males. Since there are no specific screening procedures to detect colorectal cancer or melanoma performed during the monitoring examinations, we did not create adjusted rates for these cancers.

#### Claims Data

Cancer incidence costs in the FDNY-WTCHP were calculated using the medical claims data of individuals without previous cancer diagnoses who developed cancer in 2014 or 2015 and received services through FDNY-WTCHP (N=169). We defined the initial cost of each patient's care as the sum of the amounts paid for all medical procedures and medications billed within one year after the diagnosis date.<sup>2,3</sup>

The claims data includes healthcare services that were authorized by the FDNY-WTCHP and performed by WTCHP providers. Providers submit claims for services to the FDNY claims processing team. Services are paid for by the WTCHP, which is run by the National Institute for Occupational Safety and Health (NIOSH), an agency of the Centers for Disease Control and Prevention (CDC).

#### Deaths

Death dates of WTC-exposed rescue/recovery workers were obtained from the FDNY database. These dates were utilized when calculating person-time for the 2007-2011 FDNY-WTCHP cancer rates, and to determine cohort members alive on 1/1/2012. Age-specific mortality rates, used to predict deaths in the cohort, were obtained from the National Center for Health Statistics (NCHS).<sup>4</sup>

## Statistical Analyses

We entered NYC cancer rates and NCHS death rates into simulations to estimate the 20-year cancer incidence in the study population. In each simulation, instances of cancer and death were determined by random number generators that used the Poisson distribution and each individual's demographic-specific rates. Cancer events were summed to determine the total case counts for each simulation. We performed the simulation 1,000 times for each cancer subtype to obtain mean incidence estimates and 95% confidence intervals (CIs).

For the subgroup analysis, we restricted the results from the simulations to only include cancers occurring in white males. Simulations were repeated using the calculated FDNY-WTCHP rates in place of NYC rates. To examine the possibility that some of the cancer counts produced by FDNY rates might be affected by surveillance bias, we conducted a sensitivity analysis in which we re-ran the simulations for all cancers combined and for prostate, hematologic, lung, thyroid, kidney, and bladder cancer with FDNY rates that were adjusted for possible early cancer detection.

The financial burden of incident cancer in the full cohort was approximated by multiplying the mean medical costs of initial cancer care with the 20-year case counts projected in our primary analysis; this created aggregate estimates of the direct medical costs (in 2015 dollars) of initial care from 1/1/2012–12/31/2031. Since costs of specific treatment procedures increase due to the adoption of new technologies,<sup>2</sup> our calculated mean treatment costs were increased by 2% for every year through 2031.

## eResults

### FDNY-WTCHP Population Characteristics and Cancer Diagnoses

Of the 14,474 individuals included in the main study population, 14,007 (96.8) were male, and 88.3% (12,374) of males were white. The white male subgroup was similar to the full cohort in age, smoking status, education, and WTC exposure level, but had a greater proportion of firefighters.

Between 9/11 and 12/31/2011, the most commonly diagnosed cancer type in the FDNY-WTCHP population was prostate, followed by the combined hematologic cancers, melanoma, colorectal, thyroid, bladder, and lung and kidney cancer (Table). There were too few incident cases (<20) at other cancer sites to investigate separately.

### Estimated 20-year Cancer Incidence in FDNY-WTCHP Population

When examining the future cancer incidence per five-year time interval, we observed that the number of newly occurring cases was projected to be highest during 2027-2031, the final five years (873 cases, 95% CI: 826-919). The five largest contributors to the estimated future cancer burden were prostate, lung, hematologic, colorectal and bladder cancer.

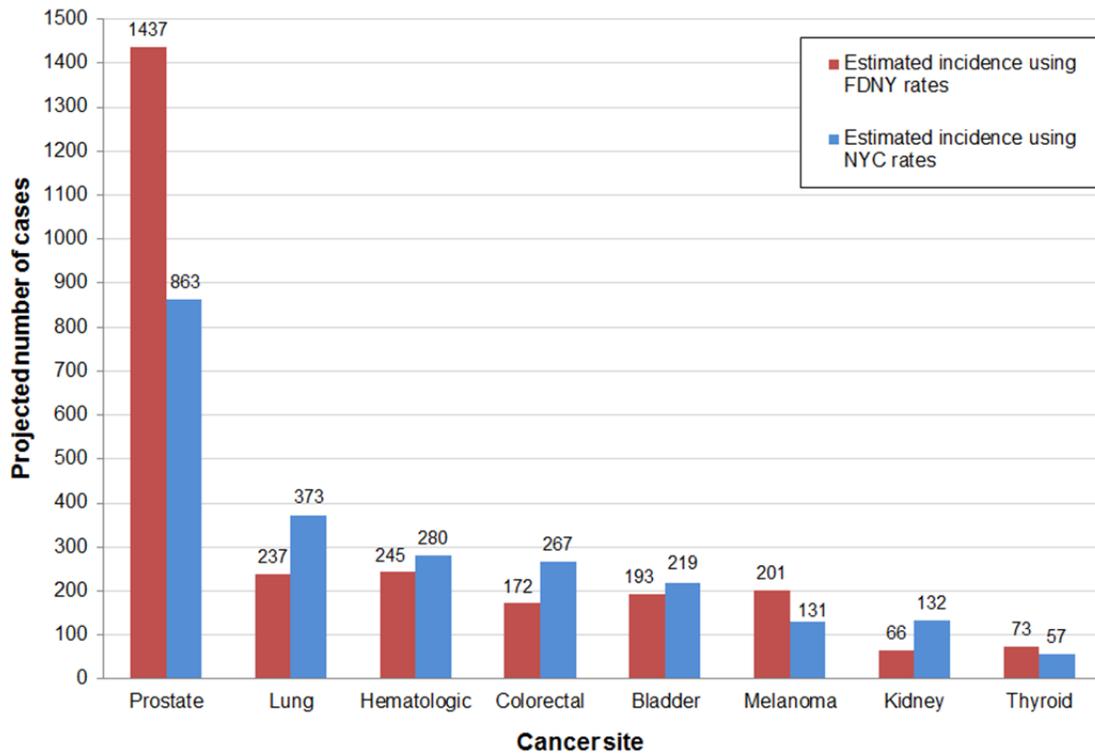
### Estimated 20-year Cancer Incidence in White Male Subgroup

While the substitution of NYC rates with FDNY rates in our subgroup analysis resulted in higher estimates of prostate cancer, thyroid cancer, melanoma, and all cancers combined, it led to lower projected numbers of lung (237 [95% CI, 212-262] vs. 373 [95% CI, 343-405]), kidney (66 [95% CI, 54-80] vs. 132 [95% CI, 114-152]), colorectal (172 [95% CI, 152-191] vs. 267 [241-292]), bladder (193 [95% CI, 171-216] vs. 219 [95% CI, 196-241]) and hematologic cancers (245 [95% CI, 220-270] vs. 280 [95% CI, ) ( $p < .01$  for all) (eFigure 1A).

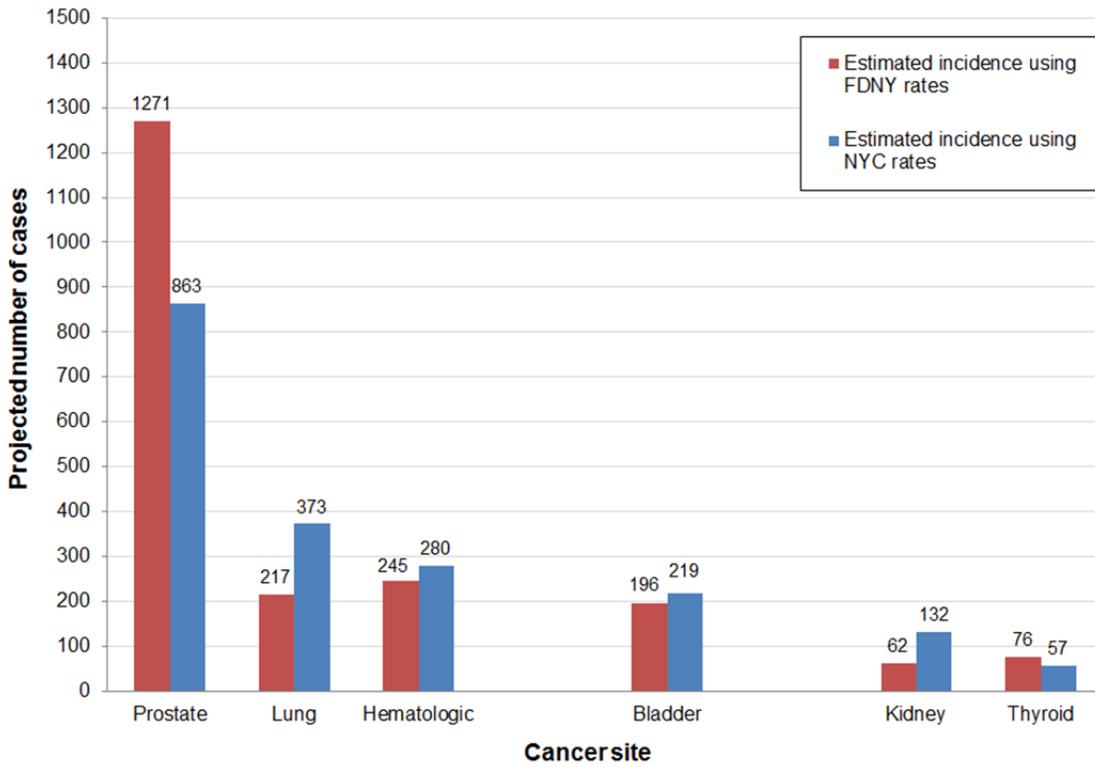
<b>eTable 1: Characteristics of WTC<sup>a</sup>-exposed FDNY<sup>b</sup> rescue/recovery workers alive and without prior cancer diagnoses on 1/1/2012</b>		
<b>Variable</b>	<b>Study cohort (N=14,474)</b>	<b>White male subgroup (N=12,374)</b>
Age group on 1/1/2012, N (%)		
25-29 years	30 (0.21)	24 (0.19)
30-34 years	556 (3.84)	394 (3.18)
35-39 years	1,358 (9.38)	1,032 (8.34)
40-44 years	2,446 (16.90)	2,025 (16.36)
45-49 years	3,005 (20.76)	2,590 (20.93)
50-54 years	2,911 (20.11)	2,610 (21.09)
55-59 years	2,249 (15.54)	2,006 (16.21)
60-64 years	974 (6.73)	821 (6.63)
65-69 years	542 (3.74)	492 (3.98)
70-74 years	284 (1.96)	269 (2.17)
75-79 years	94 (0.65)	88 (0.71)
80+ years	25 (0.17)	23 (0.19)
Race, N (%)		N/A
White (Non-Hispanic)	12,599 (87.05)	
Black	799 (5.52)	
Hispanic	981 (6.78)	
Asian	84 (0.58)	
Native American	11 (0.08)	
Sex, N (%)		N/A
Male	14,007 (96.77)	
Female	467 (3.23)	
Class, N (%)		
Firefighter	12,395 (85.64)	11,491 (92.86)
EMS <sup>c</sup>	2,079 (14.36)	883 (7.14)
Education level, N (%)		
High school	7,896 (54.55)	6,698 (54.13)
Associate's degree or RN	1,877 (12.97)	1,565 (12.65)
Bachelor's degree	3,295 (22.76)	2,955 (23.88)
Master's degree or higher	595 (4.11)	520 (4.20)
Unknown	811 (5.60)	636 (5.14)
Smoking, N (%)		
Never	9,383 (64.83)	8,125 (65.66)
Former	4,225 (29.19)	3,594 (29.04)

Current	866 (5.98)	655 (5.29)
<b>eTable 1: Characteristics of WTC<sup>a</sup>-exposed FDNY<sup>b</sup> rescue/recovery workers alive and without prior cancer diagnoses on 1/1/2012 (continued)</b>		
<b>Variable</b>	<b>Study cohort (N=14,474)</b>	<b>White male subgroup (N=12,374)</b>
WTC site arrival time, N (%)		
Morning of 9/11	2,222 (15.35)	1,833 (14.81)
Afternoon of 9/11	6,602 (45.61)	5,848 (47.26)
9/12	2,590 (17.89)	2,293 (18.53)
9/13 – 9/24	2,498 (17.26)	2,004 (16.20)
After 9/24	436 (3.01)	287 (2.32)
Unknown	126 (0.87)	109 (0.88)
WTC site work duration in months, median (IQR)	3 (1-5) <sup>d</sup>	3 (1-5) <sup>e</sup>
<sup>a</sup> World Trade Center <sup>b</sup> Fire Department of the City of New York <sup>c</sup> Emergency Medical Services <sup>d</sup> N = 14,348; 126 have unknown duration <sup>e</sup> N = 12,265; 109 have unknown duration		

**A**



**B**



**eFigure. Projected incidence of common site-specific cancers in World Trade Center (WTC)-exposed white male Fire Department of the City of New York (FDNY) rescue/recovery workers, 1/1/2012–12/31/2031.** Panel A shows the number of incident cancer cases projected to occur in WTC-exposed white male FDNY rescue/recovery workers when using calculated FDNY World Trade Center Health Program (WTCHP) cancer rates (red) and New York City cancer rates (blue), by cancer type. Panel B shows revised incidence estimates (red) for prostate, lung, hematologic, bladder, kidney and thyroid cancer after the FDNY-WTCHP rates for these cancer types were adjusted for possible surveillance bias.

<b>eTable 2: Cancer treatment costs in FDNY<sup>a</sup> WTC<sup>b</sup>-exposed cohort, 2015 dollars</b>		
<b>Cancer site</b>	<b>Initial 12-month mean cost per patient in 2014–2015 (95% CI)</b>	<b>Estimated aggregate cost, 1/1/2012–12/31/2031 (95% CI)</b>
All types	\$68,312 (\$54,335–\$82,289)	\$235,835,412 (\$187,582,227–\$284,088,597)
Prostate	\$32,200 (\$25,589–\$38,812)	\$37,718,206 (\$29,974,260–\$45,463,324)
Lung	\$127,273 (\$44,637–\$209,908)	\$62,174,556 (\$21,805,769–\$102,542,855)
Hematologic <sup>c</sup>	\$129,471 (\$66,438–\$192,504)	\$47,105,216 (\$24,172,026–\$70,038,407)
Colorectal	\$77,780 (\$32,793–\$122,767)	\$27,686,552 (\$11,672,989–\$43,700,115)
Melanoma	\$15,548 (\$10,584–\$20,513)	\$2,350,544 (\$1,600,087–\$3,101,151)
Bladder	\$23,723 (\$2,904–\$44,542)	\$6,364,290 (\$779,071–\$11,949,510)
Kidney	\$30,861 (\$22,768–\$38,954)	\$5,079,519 (\$3,747,464–\$6,411,410)
Thyroid	\$25,470 (\$14,987–\$35,953)	\$1,753,887 (\$1,032,018–\$2,475,756)
<sup>a</sup> Fire Department of the City of New York <sup>b</sup> World Trade Center <sup>c</sup> Includes Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, multiple myeloma, and other hematopoietic cancers.		

## eReferences

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