Registry-Based Case–Control Study of Cancer in California Firefighters

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Background *There is no consensus whether firefighters are at increased cancer risk for particular cancers. Previous studies have been small, mostly investigated cancer mortality, and suggested increased risks for brain, bladder, testicular, prostate, thyroid and colo-rectal cancers, leukemia, and melanoma.*

Methods *Records of all male cancers registered in California during 1988–2003 were obtained. Firefighters were identified from occupation and industry text fields. Logistic regression analysis used other cancers as controls.*

Results *Of the 804,000 eligible records, 3,659 had firefighting as their occupation. Firefighting was associated with testicular cancer (odds ratio = 1.54, 95% confidence interval: 1.18–2.02), melanoma (1.50, 1.33–1.70), brain cancer (1.35, 1.06–1.72), esophageal cancer (1.48, 1.14–1.91), and prostate cancer (1.22, 1.12–1.33).*

Conclusions *Use of other-cancer controls and lack of an occupational history may have biased relative risks towards the null. However, this study, which contained more firefighter cancers than any previous epidemiologic study, produced evidence supporting some prior hypotheses.* Am. J. Ind. Med. 50:339–344, 2007. *© 2007 Wiley-Liss, Inc.*

KEY WORDS: California; cancer risk; case–control studies; epidemiology; firefighters

INTRODUCTION

Firefighters are exposed to numerous combustion products. These include polycyclic aromatic hydrocarbons (PAHs), formaldehyde, benzene, chromium compounds, dioxins, asbestos, particulates and arsenic, all of which are known or strongly suspected carcinogens [IARC, 1995; Wogan et al., 2004]. Relative exposures to these chemicals will vary depending on the source of the fire, its heat, meteorologic conditions at the time, and the specific activities of the firefighter. Although it is currently common for firefighters to wear self-contained breathing apparatus (SCBA) during actual fire fighting, depending on the nature of the fire and the amount of physical activity demanded of the firefighter, SCBAs are generally not worn during the period *after* the fire, known as ‘‘overhaul’’, when firefighters pull apart walls, ceilings and floors, and remove furniture, to find and extinguish hidden fires. The overhaul can last several hours, during which substantial exposure to combustion products occurs [Bolstad-Johnson et al., 2000].

These exposures have led to concerns about occupational cancer risks associated with firefighting. Many epidemiologic studies, mainly cohort studies, have investigated whether firefighters are at increased cancer risk. However, no consensus on particular cancers has yet been reached. Most studies have been small and have examined cancer mortality, but not incidence. Mortality studies have suggested firefighters may be at risk for, in particular, brain, bladder and colo-rectal cancers, leukemia, non-Hodgkin's lymphoma, multiple myeloma, and malignant melanoma [Howe and Burch, 1990; Golden et al., 1995; Guidotti, 1995; Haas et al., 2003; LeMasters et al., 2006]. More recent studies examining cancer *incidence* in firefighters have

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suggested increased risks for testicular and thyroid cancers, cancers with low fatality rates, may also occur [Bates et al., 2001; Stang et al., 2003; Ma et al., 2006].

As a result of the increasing use of new building materials, particularly synthetic polymers, firefighter combustion product exposures may have been changing both qualitatively and quantitatively in the last few decades [Guidotti, 1995]. Therefore, the results of the firefighter studies carried out in the 1970s and 1980s may no longer be relevant to the more recent generation of firefighters.

The California Cancer Registry is one of the largest cancer registries in the world and has had statewide coverage since 1988. Ninety-four percent of the registered cancers have histological confirmation. For each incident cancer case, the registry records a text field for occupation and for industry. This is intended to record the occupations and industries in which the cancer case has had longest employment, as reported by the patient. The objective of this study was to use these text fields to examine whether they provided evidence that California firefighters were at increased cancer risk relative to other occupations, particularly for the cancer types that have previously been linked with firefighting.

METHODS

This was a registry-based case–control study. The protocol was approved by the Committee for Research on Human Subjects at the University of California, Berkeley. The study was limited to males because preliminary investigation of corresponding female cancer data found only 49 women who were recorded as having worked as a firefighter.

Data Collection and Preparation

Anonymized records of all male cancers registered by the California Cancer Registry for 1988–2003 were obtained from the Registry. These records included text fields for occupation and industry, tumor classification variables, demographic variables (age, race, sex, and county and zip code of residence) and a variable for socio-economic status. Creation of the latter variable has been described in detail elsewhere [Yost et al., 2001]. Briefly, the variable was created by the California Cancer Registry from 1990 census data at the level of the census block (about 1,000 residents). Seven socio-economic indicator variables for census blocks were combined into a single SES index using principal components analysis. Standardized component scores for the SES index were categorized into quintiles of the 21,000 California census blocks. For the purposes of this analysis, each subject was allocated to the quintile of the census block in which he lived.

To identify firefighters for our analysis, the occupation and industry fields were searched for relevant text strings that included ''fire'', such as ''firefighter'', ''fire fighter'', ''fireman'', ''fire man'', and ''fire chief''. Anyone who indicated that they worked for a fire department, but did not indicate they carried out firefighting was not considered to be a firefighter for the purposes of the analysis, as many fire department employees hold administrative positions. No information was available on how long, at what age, or during which calendar period a person worked as a firefighter.

Data Analysis

Logistic regression analysis was carried out separately for each of the suspected cancers, as well as any cancer type for which more than 50 cases were reported in firefighters, using firefighting occupation as the exposure of interest. Logistic models were adjusted by age (5-year categories), year of diagnosis (four 4-year categories), ethnicity (5 categories), and the indicator of socio-economic status (5 categories). For each model, all other cancers were used as the controls. However, if these other cancers share firefighting occupation as an etiology (or even a protective factor) with the cancer type forming the cases, then some bias in the odds ratios will result. Therefore, based on results of an initial analysis, cancers likely to be influential were excluded from the control groups used in the final logistic regression models. Analysis was limited to male subjects aged 21–80 at diagnosis.

To investigate the hypothesis that more recent exposures lead to different firefighting risks we compared risks for cancers reported during 1988 to 1995 with the corresponding risks for cancers reported in 1996–2003, while limiting these analyses to individuals aged 21–60. The latter restriction was to restrict individuals included in the analysis to those with more recent exposures.

RESULTS

There were 1.1 million records of male cancer cases obtained. Of these, 140,000 (13%) were discarded because of no recorded occupation or industry. A total of 804,107 of the remaining subjects aged 21–80 at cancer diagnosis were retained for this analysis. Of these, 3,659 had firefighting recorded as their main occupation (including retired firefighters). Table I shows basic descriptive statistics for these individuals, firefighters, and non-firefighters. The main difference apparent between the groups is that firefighters tend to be overwhelmingly recorded as non-Hispanic whites (91.4%), relative to other California cancer cases (75.3%), which have a more mixed racial/ethnic distribution.

Separate logistic regression analyses were carried out for each cancer type for which there had been more than

TABLE I. Demographic Characteristics of Firefighter and Non-firefighter Cancer Cases, California Cancer Registry, 1988–2003

Characteristic	Firefighters Number	Firefighters Percent	Non-firefighters Number	Non-firefighters Percent
Age at diagnosis				
• 21–30	67	2.10	19,499	2.44
• 31–40	185	5.06	40,472	5.06
• 41–50	361	9.87	73,209	9.15
• 51–60	821	22.4	153,775	19.22
• 61–70	1307	35.7	272,290	34.08
• 71–80	908	24.8	240,703	30.07
Race/ethnicity				
• Non-Hispanic white	3,345	91.42	602,763	75.30
• Non-Hispanic black	79	2.16	53,653	6.69
• Hispanic	178	4.86	86,143	10.76
• Asian/Pacific Islander	31	0.85	47,174	5.89
• American Indian/Alaskan native	1	0.03	888	0.11
• Other/unknown	25	0.68	9,917	1.24
Socio-economic quintile of residence				
• 1 (lowest)	231	6.31	107,124	13.38
• 2	628	17.16	147,462	18.42
• 3	843	23.04	167,107	20.88
• 4	1,003	27.41	179,775	22.46
• 5 (highest)	954	26.07	198,980	24.86
Year of diagnosis				
• 1988–1991	742	20.28	193,028	24.11
• 1992–1995	917	25.06	219,854	27.47
• 1996–1999	985	26.92	190,896	23.85
• 2000–2003	1,015	27.74	196,670	24.57
Total	3,659	100	800,448	100

50 cancers recorded in firefighters, as well as any other cancer types for which there were prior hypotheses. The only two cancers in this latter category were thyroid cancer (32 cases) and multiple myeloma (37 cases). Cancers investigated and the numbers of cases in firefighters are shown in Table II.

Table II also shows (under ‘‘No control exclusions’’) the results for each analysis when all other cancers were included in the control group for each model. Based on these analyses, it was decided to exclude as controls from the final models cancers of the lung and bronchus, bladder and prostate, colo-rectal cancers, and skin melanomas. These were cancers with substantial numbers of cases and which, in the initial models, showed evidence of associations (in either direction) with firefighting occupation. Results for the models with control exclusions are shown in the last two columns of Table II (under ‘‘Control exclusions’’).

Of the hypothesized cancers (see INTRODUCTION), the analysis produced evidence that firefighting as an occupation was a risk factor for testicular cancer (odds ratio = 1.54, 95% confidence interval: 1.18–2.02), melanoma (1.50, 1.33–1.70), brain cancer (1.35, 1.06–1.72), leukemias (1.22, 0.99–1.49), prostate cancer (1.22, 1.12–1.33), and possibly thyroid cancer (1.17, 0.82–1.67). The risk for esophageal cancer, not previously suggested as being associated with firefighting, was also raised (1.48, 1.14–1.91). There was little or no evidence for increased risk for bladder cancer, non-Hodgkin’s lymphoma, multiple myeloma, colorectal cancer or lung cancer.

Cancer trends were investigated by separating cancer registrations into the periods 1988–1995 and 1996–2003. Odds ratios for these two periods were calculated after restricting the analysis to subjects aged 21–60 at diagnosis. Results are shown in Table III. With the possible exception of skin melanoma and esophageal cancer, there was little evidence of an increasing trend with time. Odds ratios for some cancers (e.g., testicular and brain cancers) were lower in the second period. However, interpretation of this table is limited by the small numbers of firefighters with any particular cancer type and lack of knowledge of periods of firefighting service.

TABLE II. Results of Logistic Regression Analyses, with and without Control Exclusions

			No control exclusions		Control exclusions[b]	
Cancer site	SEER codes[a]	Number of firefighters	OR[c]	95% CI	OR[c]	95% CI
Esophagus	21010	62	1.37	1.06–1.76	1.48	1.14–1.91
Stomach	21020	51	0.77	0.58–1.02	0.80	0.61–1.07
Cecum	21041	52	1.03	0.78–1.35	1.09	0.82–1.44
Colo-rectal	21043–8	282	0.84	0.74–0.94	0.90	0.79–1.03
Pancreas	21100	63	0.85	0.66–1.09	0.90	0.70–1.17
Lung & bronchus	22030	495	0.92	0.84–1.01	0.98	0.88–1.09
Melanoma–skin	25010	323	1.44	1.28–1.62	1.50	1.33–1.70
Prostate	28010	1,144	1.20	1.12–1.29	1.22	1.12–1.33
Testis	28020	70	1.34	1.04–1.74	1.54	1.18–2.02
Bladder	29010	174	0.79	0.68–0.92	0.85	0.72–1.00
Kidney & renal pelvis	29020	101	0.98	0.81–1.20	1.07	0.87–1.31
Brain	31010	71	1.23	0.97–1.56	1.35	1.06–1.72
Thyroid	32010	32	1.06	0.75–1.51	1.17	0.82–1.67
Non-Hodgkin's lymphoma	33041–2	159	0.98	0.84–1.15	1.07	0.90–1.26
Multiple myeloma	34000	37	0.97	0.70–1.34	1.03	0.75–1.43
Leukemias	35011–43	100	1.13	0.92–1.37	1.22	0.99–1.49

[a]Surveillance Epidemiology and End Results (SEER) codes available at: http://seer.cancer.gov/siterecode/icdo3.d01272003/.
[b]Excluded from control groups were cancers of the lung and bronchus, bladder and prostate, colo-rectal cancers, and skin melanomas.
[c]All models adjusted for age, calendar period of diagnosis, race, and an indicator of socio-economic status for the census block of residence.

DISCUSSION

With the exception of a previous study of mortality in San Francisco firefighters [Beaumont et al., 1991], this has been the first study of cancer risks in California firefighters. The analysis, using a larger number of incident cancer cases in firefighters than any other study, has provided confirmation of some existing hypotheses about occupational cancers of firefighters. Most notably the analysis supports previous results that firefighting may be associated with cancers of the testes [Bates et al., 2001; Stang et al., 2003; Ma et al., 2006], prostate [Grimes et al., 1991; Demers et al., 1994] and brain [Vena and Fiedler, 1987; Grimes et al., 1991; Demers et al., 1992; Aronson et al., 1994; Burnett et al., 1994], and melanoma of the skin [Sama et al., 1990; Bates et al., 2001]. There is also evidence of an association with esophageal cancer and possibly leukemia.

This study had the advantage of a large number of cases with histological confirmation of diagnosis and controls were representative of the population that generated the cases. However, there were several limitations. First, there is some potential for bias, particularly from use of other cancer cases as controls. If these controls shared a common etiology with the cancer of interest, then this would have biased odds ratios towards the null. An attempt was made to reduce this by excluding some cancer types from the control groups, but we can never be completely confident that all such selection bias has been eliminated.

The second limitation was the reliance on incompletely recorded text fields for identification of firefighter status. A substantial proportion of cases recorded in the cancer registry had missing data for both occupation and industry fields and recording of details was unstandardized and limited to a few words. These fields were intended to record the occupation and industry in which the subject had worked for the longest time (as reported by the subject himself). However, we had no information on actual length of time worked as a firefighter. Despite the potential for misclassification, designation of a cancer case as a firefighter for the purposes of this study was carried out blind to cancer type. Assuming that accuracy of recording of occupation and industry was not differential by cancer type (conditional on age) exposure misclassification would be expected to have biased odds ratios towards the null.

It is likely that some of the individuals designated as non-firefighters (the "unexposed") will have worked or volunteered as firefighters at some time in their careers. However, it is probably reasonable to assume that this would have been the case for only a small proportion of the unexposed subjects. That being the case, the effect on odds ratios would be slight, but again probably towards the null.

Thirdly, we had only limited data on potentially confounding covariates, and no data on tobacco consumption. However, the low odds ratios for both lung and bladder cancer found in this study confirm other results that firefighters do not have high smoking rates [Peters et al.,

TABLE III. Comparison of Results for 1988–1995 and 1996–2003 in Subjects Aged 21–60

		1988–1995			1996–2003		
Cancer site	SEER codes[a]	No.[b]	OR[c]	95% CI	No.[b]	OR[c]	95% CI
Esophagus	21010	8	1.36	0.67–2.78	15	1.86	1.10–3.14
Stomach	21020	13	1.31	0.75–2.99	7	0.64	0.30–1.36
Cecum	21041	6	1.07	0.48–2.43	8	1.16	0.58–2.36
Colo-rectal	21043–8	48	1.14	0.83–1.56	62	1.18	0.89–1.55
Pancreas	21100	11	1.16	0.63–2.13	9	0.74	0.38–1.45
Lung & bronchus	22030	62	0.85	0.64–1.14	47	0.77	0.56–1.05
Melanoma–skin	25010	74	1.55	1.19–2.01	128	1.86	1.51–2.29
Prostate	28010	89	1.46	1.12–1.91	214	1.55	1.28–1.88
Testis	28020	37	1.92	1.32–2.80	32	1.29	0.87–1.92
Bladder	29010	18	0.71	0.44–1.14	27	0.94	0.63–1.40
Kidney & renal pelvis	29020	24	1.47	0.96–2.24	22	0.87	0.57–1.35
Brain	31010	22	1.63	1.05–2.52	19	1.08	0.68–1.72
Thyroid	32010	12	1.54	0.86–2.76	14	1.15	0.67–1.98
Non-Hodgkin's lymphoma	33041–2	42	1.03	0.74–1.43	38	0.94	0.67–1.32
Multiple myeloma	34000	9	1.85	0.95–3.61	10	1.41	0.75–2.65
Leukemias	35011–43	18	1.18	0.73–1.90	19	1.06	0.67–1.69

[a]Surveillance Epidemiology and End Results (SEER) codes available at: http://seer.cancer.gov/siterecode/icdo3.d01272003/
[c]Number of firefighters with cancer type.
[b]All models adjusted for age, calendar period of diagnosis, race, and an indicator of socio-economic status for the census block of residence. Excluded from control groups were cancers of the lung and bronchus, bladder and prostate, colo-rectal cancers, and skin melanomas.

1974; Bates, 1987; Stellman et al., 1988]. Although we were able to adjust our analyses for socio-economic status, this variable was based on the socio-economic status of the area where the person lived and can be expected to have misrepresented the actual socio-economic status of some individuals.

Our analysis would also, of course, have greatly benefited from availability of data on firefighting histories, including job type, exposures and length of service as a firefighter. This would have permitted subgroup and trend analyses, which would have enhanced causal inference.

There are few well-established risk factors for prostate, testicular or brain cancers, for which this study and others suggest increased risks in firefighters. Esophageal cancer has been associated with both alcohol and tobacco consumption, as well as with dietary nitrosamine exposure [Nyrén and Adami, 2002]. Nitrosamines can be present in smoke from combustion processes. Melanoma is known to be caused by exposure to ultraviolet rays of the sun. It is possible that, as a consequence of their profession, firefighters have high sun exposure relative to the general population. All of these cancer types have had other occupational associations, although they have often not been consistent across studies [Nyrén and Adami, 2002; Savitz and Trichopoulos, 2002; Signorello and Adami, 2002; Tamimi and Adami, 2002].

In conclusion, this study has added to the evidence that firefighters are at increased risk for certain cancers, particularly testicular and brain cancers and melanoma of the skin. However, final resolution of the question of whether firefighters are at increased occupational cancer risk will probably require a large occupational cohort study followed by an appropriate nested case-control study (probably with several cancer endpoints) that combines several exposure assessment methods, including work records and questionnaires to collect detailed covariate data. However, reconstruction of firefighting exposure histories will be challenging. Most of the approximately 25 other published investigations of cancer in firefighters have been cohort studies and relatively small. To date, none of these cohort studies has been followed by a nested case–control study.

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