Review of the Epidemiologic Studies for the Association between Firefighters and Selected Cancers;

Multiple Myeloma, Stomach, Prostate, Testicular, Intestinal - Colon and Rectal Cancers

Technical Report Number 74-1-2007
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David Bonauto, MD, MPH
Barbara Silverstein, PhD, MPH, CPE

Safety and Health Assessment and Research for Prevention (SHARP) Program,
Washington State Department of Labor and Industries, P.O. Box 44330,
Olympia, Washington, 98504-4330.

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Review of the Epidemiologic Studies for the Association between Firefighters and Selected Cancers; Multiple Myeloma, Stomach, Prostate, Testicular, Intestinal - Colon and Rectal Cancers.

Summary:

In 2002, inclusion of different cancers for presumption for fire fighters relied on evidence from at least three independent studies reporting statistically significant increased risk for firefighters of ≥1.5 times that of the reference population. The current review considers all relevant studies where cancer risk was assessed and also considers the relationship between science and public policy. It is noted that public health policy traditionally has not waited for definitive science when there is a reasonable chance that the consequences of inaction would lead to serious harm. This document summarizes what is known from epidemiological studies to date in order to inform public policy makers.

Introduction:

Washington State is one of many states with firefighter presumption laws. In 1987, presumption was granted for firefighters for respiratory disease (RCW 51.32.185). In 2001, with the introduction of an expanded firefighter presumption statute to include all cancers, the primary review of the peer-reviewed literature for cancer presumption was based on the combination of the following three criteria:

- There was a statistically significant increased association between firefighting and cancer,
- The association demonstrated that firefighters had twice the risk of the comparison population, and
- The findings were consistent across at least three independent studies.

In 2002, the cancers where the strength of the association was suspected of being 1.5 – 2.0 times more common in firefighters relative to the referent population were included in legislation. Cancers included into RCW 51.32.185 were primary brain cancer, leukemia, non-Hodgkins lymphoma, kidney, ureter, bladder, and melanoma.

In 2007, the legislature is considering (1833/5741) expanding the presumption to include stomach cancer, intestinal cancer (colon/rectal), prostate cancer, testicular cancer and multiple myeloma.

This again reviews the association between firefighters and selected cancers. This review does not consider the biologic plausibility of exposure and disease. Information on research studies demonstrating the strength of an association is presented. The available information on exposure response relationships is presented. Often information on an exposure-response trend is either missing or the number of cancers in the study is insufficient to provide such information. We reviewed studies available in the peer-reviewed literature. A comprehensive list of research studies is available in LeMasters (2006) and in the reference section.

Review of Research Studies:

The following charts represent a summary of epidemiologic studies published in the peer-reviewed literature regarding firefighters and selected cancers in HB 1833 and SB 5741 –multiple myeloma, stomach, prostate, testicular, and intestinal - colon and rectal - cancers.

For the charts presented, the estimate of the increased or decreased risk to firefighters is at the top of each column of the histogram (the point estimate). The 95% confidence interval from that estimate is represented by the lines. In order to be considered a statistically significant result the lower confidence interval should not cross 1.0.

There are several types of studies and common abbreviations used. Each is expressed such that a point estimate of 1.0 represents the observed value in the firefighter population being what is expected from estimates from the referent population.

SMR = Standardized Mortality Ratio
SIR = Standardized Incidence Ratio
OR = Odds Ratio
PMR = Proportionate Mortality Ratio

Generally, the study designs associated with deriving an SMR or SIR are more robust studies, whereas studies that determine an OR or a PMR are less robust. Some cancers are rare or do not result in mortality (i.e. testicular cancer) and study design are often guided by such – therefore in these cases SIR studies are more appropriate to review for association.

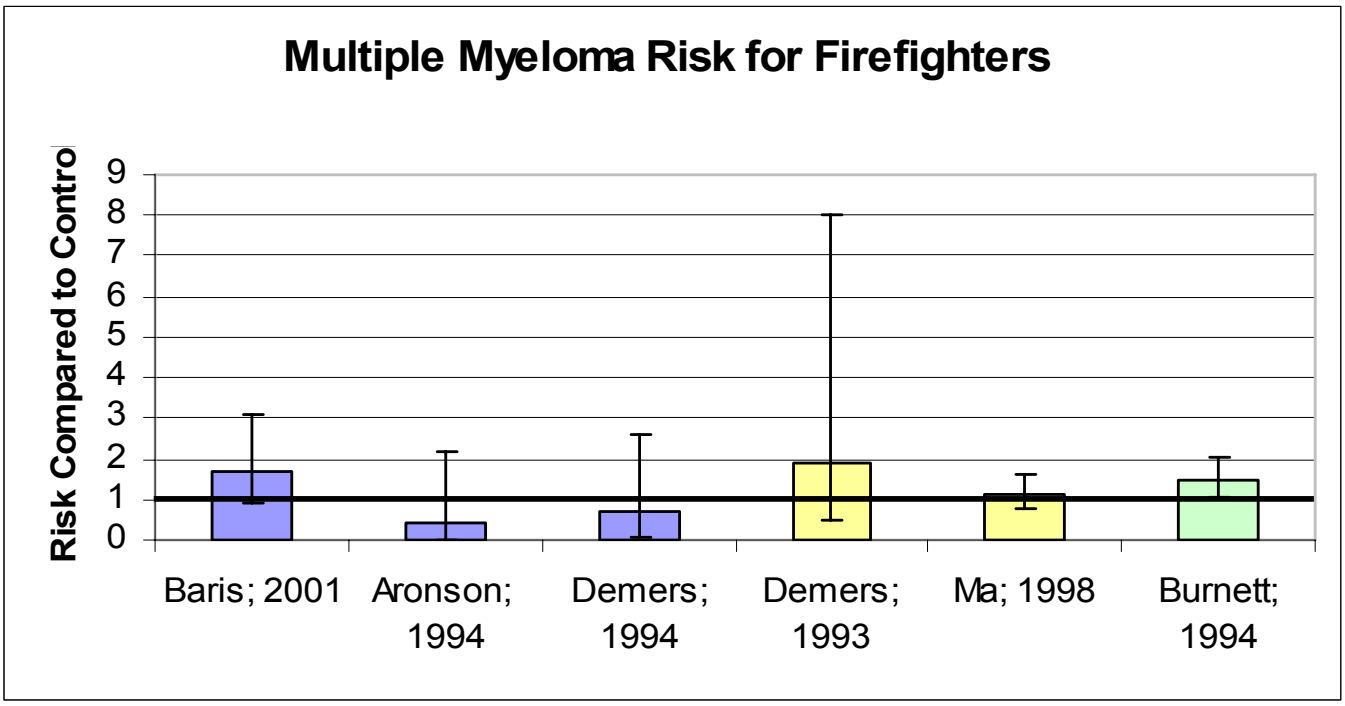
The annual number of cases can be estimated using the Washington State Cancer Registry data (Table A). The number of cases expected per year depends on the estimate of the increased risk for cancer in firefighters.

Table A: Estimated Number of Cancer Cases. Estimated Incidence Rate per 100,000 WA residents aged 30-64 year olds based on 1999-2003 annual average incidence rates from the Washington State Cancer Registry (http://www3.doh.wa.gov/WSCR/ASP/WSCRQryAS.asp)

Cancer Type	Sex	Expected Rate per 100,000 Residents	Population at risk*	# Annual Cancer Cases*	Annual # for FF if 1.5 times risk
Colorectal	Male	38.8	4150	1.610	2.415
	Female	28.7	219	0.063	0.094
Stomach	Male	6.2	4150	0.257	0.386
	Female	2.9	219	0.006	0.010
Multiple Myeloma	Male	4.8	4150	0.199	0.299
	Female	2.8	219	0.006	0.009
Prostate	Male	113.3	4150	4.702	7.053
Testicular	Male	9.1	4150	0.378	0.566

* Estimates that there are ~7,000 Firefighters in WA State of which only ~62.4% meet 10 years eligibility; Assumes ratio of 95% male / 5% female firefighters. Total at risk = 4369 firefighters (4150 men; 219 women); Assumes almost all firefighters retire by age 60.
This estimate is for illustration purposes only and does not include existing cases of the specific cancer.

Results: Individual Cancers



Purple shading are cohort studies (SMR, SIR, RR); Yellow shading are case control studies; Green shading are studies reporting proportionate mortality ratios (PMR).

- Results of an association between firefighting and multiple myeloma are inconsistent across studies.[1]
- Statistically significant increased risk of multiple myeloma is present in the study by Burnett (PMR 1.48); the study by Baris approached statistical significance with an SMR estimate of 1.68 (0.90-3.11).
- Dubrow and Wegman (1983) reported a statistically significant 'aggregate observed-expected ratio' of 2.04. The data was part of a survey of >200 occupational categories to explore occupational cancers.
- Heyer et. al. (1992) reported an SMR of 2.25 (0.47-6.60) for 'Other lymphatic/hematopoetic cancers'. Two of the three cancers were identified as multiple myeloma with both cases occurring in the population of firefighters with >30 years of service SMR 9.89 (1.2-35.71).
- A recent study by McMasters (2006) reported a summary risk estimate from several published studies - this study uses a methodology which was not used by WA State to determine if cancers were associated with firefighting. This analysis reports the following risk estimates for multiple myeloma:
  - Meta SMR – 1.69 (1.08 – 2.51)
  - Meta SIR – 1.42 (1.04 – 1.89)
  - Meta Summary – 1.53 (1.21 – 1.94)
- Risk factors reported by the National Cancer Institute for multiple myeloma include increasing age, race and history of related medical disorders. Other than age, these factors are not controlled in the research studies and are only relevant if the risk factor is either more or less present in firefighters compared to the referent population.
- All studies are potentially limited by one or more of the following: small size of the study population, the small number of cases, potential misclassification of occupation at the time of death, the control of the presence or absence of other cancer risk factors, limitations of the exposure measures to general occupation, the general health status of firefighters compared to the referent population (i.e. the healthy worker effect and the inclusion of non-employed individuals in the referent group, and other study design limitations.
- The Washington State Occupational Mortality Database, at http://www3.doh.wa.gov/OCCMORT/, for all Washington State deaths from 1950-1999 reports a PMR of 0.95 for male firefighters and multiple myeloma. The result did not meet statistical significance. No data is available for female firefighters.

[1] The upper confidence interval for Demers et al; 1993 was truncated to allow readability of the graph. OR 1.9 (95% CI 0.5 – 9.4)

Multiple Myeloma and Evidence for a Dose-Response Trend:

The evidence for an exposure – response trend is presented below. Generally, studies are controlled for age of the firefighter and referent population. Age is a confounder in multiple myeloma studies and is generally controlled for in the analysis phase.

Table B: Multiple Myeloma and Measures of Exposure-Response Relationship

Duration of Employment

Baris; 2001	**≤ 9 years**	**10 - 19 years**	**≥ 20 years**
Cases	1	3	6
SMR	0.73 (0.10 - 5.17)	1.50 (0.48 - 4.66)	**2.31 (1.04 - 5.16)**

Demers; 1993	**< 10 years**	**10 + years**
Cases	1	4
OR	0.9 (0.00 - 22.3)	2.9 (0.4 - 21.6)

Date of Hire

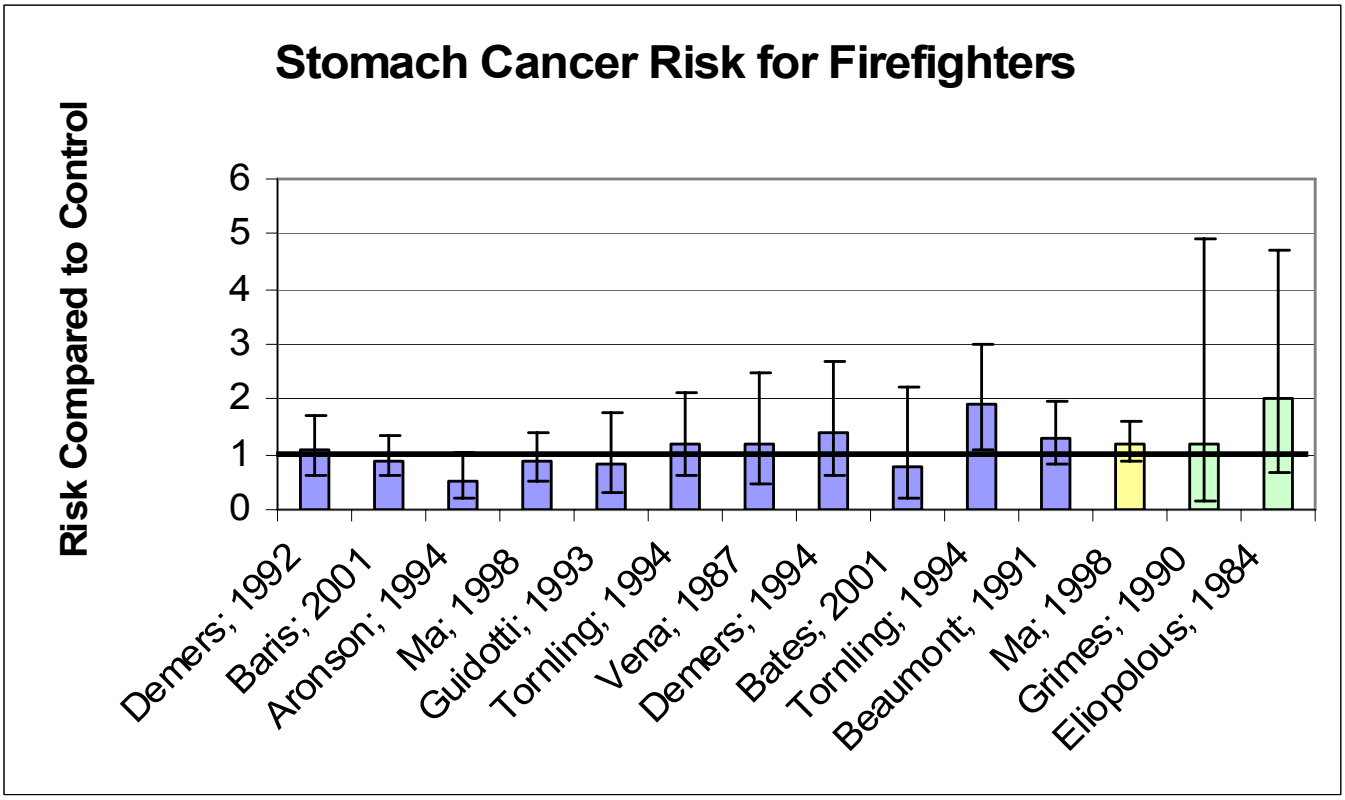
Baris; 2001	**< 1935**	**1935 - 1944**	**> 1944**
Cases	4	3	3
SMR	2.06 (0.77 - 5.49)	1.43 (0.46 - 4.42)	1.56 (0.50 - 4.84)

Number of Runs

Baris; 2001	**Low (<3,323 runs)**	**Medium**	**High (≥ 5,099 runs)**
Cases	1	3	2
SMR	0.57 (0.88 - 4.06)	2.69 (0.87 - 8.35)	1.73 (0.43 - 6.90)

Age of Occurrence

Burnett; 1994	**Under Age 65**
Cases	11
PMR	1.36 (0.68 - 2.43)



Purple shading are cohort studies (SMR, SIR, RR); Yellow shading are case control studies; Green shading are studies reporting proportionate mortality ratios (PMR).

- Results of an association between firefighting and stomach cancer are inconsistent across studies.[2]
- Tornling (1994) reported a statistically significant increased incidence of stomach cancer in firefighters with a SIR of 1.92 (1.14-3.04).
- A recent study by McMasters (2006) reported a summary risk estimate from several published studies - this study uses a methodology which was not used by WA State to determine if cancers were associated with firefighting. This analysis reports the following risk estimates for stomach cancer:
  - Meta SMR – 0.92 (0.73 – 1.16)
  - Meta SIR – 1.58 (1.12 – 2.16)
  - Meta RR – 1.21 (0.80 – 1.81)
  - Meta Summary – 1.22 (1.04 – 1.44)
- Risk factors reported by the National Cancer Institute for stomach cancer include increasing age, gender, race, diet, smoking, family history, and helicobacter pylori. Other than age, these factors are not controlled in the research studies and are only relevant if the factor is either more or less present in firefighters compared to the referent population.
- All studies are potentially limited by one or more of the following: small size of the study population, the small number of cases, potential misclassification of occupation at the time of death, the control of the presence or absence of other cancer risk factors, limitations of the exposure measures to general occupation, the general health status of firefighters compared to the referent population (i.e. the healthy worker effect and the inclusion of non-employed individuals in the referent group, the presence or absence of stomach cancer risk factors –diet, nationality or others), and other study design limitations.
- The Washington State Occupational Mortality Database, at http://www3.doh.wa.gov/OCCMORT/, for all Washington State deaths from 1950-1999 reports a PMR of 0.98 for male firefighters and stomach cancer. The result did not meet statistical significance. No data is available for female firefighters.

[2] The upper confidence interval for Grimes et al; 1990 was truncated to allow readability of the graph. PMR 1.17 (95% CI 0.17 – 8.2)

Stomach Cancer and Evidence for an Exposure-Response Trend:

The evidence for an exposure – response trend is presented below. Generally, studies are controlled for age of the firefighter and referent population. Age and gender are confounders in stomach cancer studies and is generally controlled for in the analysis phase. Smoking is an uncontrolled confounder in these analyses.

Table C: Stomach Cancer and Measures of an Exposure-Response Relationship

Duration of Employment

Baris; 2001	≤ 9 years	10 - 19 years	≥ 20 years
Cases	4	14	6
SMR	0.55 (0.21 - 1.48)	1.39 (0.83 - 2.35)	0.65 (0.29 - 1.44)

Beaumont; 1991	3 - 9 years	10 - 19 years	20 - 29 years	30 + years
Cases	2	2	8	11
RR	1.56	1.15	1.03	1.67

Demers; 1994	≤ 10 years	10 - 19 years	20 - 29 years	30 + years
Cases	2	1	4	1
SIR	3.0 (0.4 - 11)	1.2 (0.0 - 6.9)	1.1 (0.3 - 2.9)	1.4 (0.0 - 8.1)

Tornling; 1994	≤ 20 years	20 - 30 years	> 30 years
Cases	1	5	12
SIR	1.02 (0.1 - 5.68)	1.18 (0.38 - 2.75)	**2.86 (1.49 - 5.05)**

Date of Hire

Baris; 2001	< 1935	1935 - 1944	> 1944
Cases	17	4	3
SMR	1.19 (0.74 - 1.92)	0.60 (0.22 - 1.59)	0.54 (0.18 - 1.67)

Number of Runs

Baris; 2001	Low (<3,323 runs)	Medium	High (≥ 5,099 runs)
Cases	4	1	2
SMR	0.66 (0.25 - 1.75)	0.31 (0.05 - 2.22)	0.66 (0.16 - 2.63)

Fires

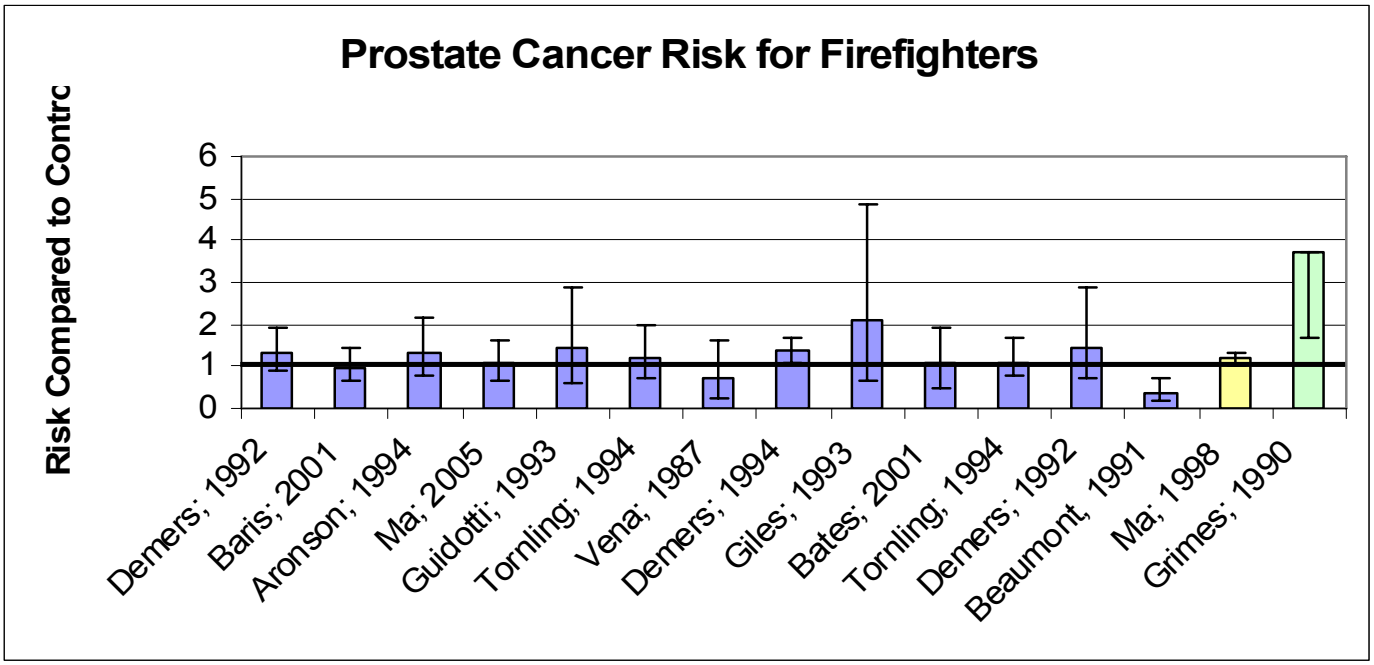
Tornling; 1994	< 800	800 - 1000	≥ 1000
Cases	2	4	12
SIR	1.04 (0.12 - 3.76)	1.37 (0.37 - 3.52)	**2.64 (1.36 - 4.61)**

Time since First Employment

Beaumont; 1991	3 - 19 years	20 - 29 years	30 - 39 years	40 + years
Cases	2	1	5	14
RR	1.31	0.26	0.91	**2.32**

Demers; 1994	< 20 years	20 - 29 years	30 + years
Cases	0	2	6
SIR	0.0 (0.0 - 15.7)	2.3 (0.3 - 8.3)	1.3 (0.5 - 2.8)

Tornling; 1994	< 30 years	30 - 40 years	40 + years
Cases	5	12	1
SIR	**4.81 (1.55 - 11.22)**	**6.06 (3.13 - 10.59)**	0.16 (0.0 - 0.88)



Purple shading are cohort studies (SMR, SIR, RR); Yellow shading are case control studies; Green shading are studies reporting proportionate mortality ratios (PMR).

- Results of an association between firefighting and prostate cancer are inconsistent across studies.[3]
- A statistically significant increased risk of prostate cancer was observed in one cohort study with a SIR of 1.4 x of the population referent risk (Demers; 1994). One PMR study by Grimes in Honolulu firefighters indicated an increased risk of 3.7 times of the referent population. The odds ratio in a case control study by Ma (1998) was statistically significant and suggested a 20% increased risk of firefighters for prostate cancer.
- Beaumont (1991) reported a statistically significant decreased prostate cancer risk - SIR 0.38 (0.16 – 0.75).
- A recent study by McMasters (2006) reported a summary risk estimate from several published studies - this study uses a methodology which was not used by WA State to determine if cancers were associated with firefighting. This analysis reports the following risk estimates for prostate cancer:
    - Meta SMR – 1.14 (0.93 – 1.39)
    - Meta SIR –1.29 (1.09 – 1.51)
    - Meta RR – 0.78 (0.13 – 4.82)
    - Meta Summary – 1.28 (1.15 – 1.43)
- Risk factors reported by the National Cancer Institute for prostate cancer include increasing age, race, and diet. Other than age, these factors are not controlled in the research studies and are only relevant if the factor is either more or less present in firefighters compared to the referent population.
- All studies are potentially limited by one or more of the following: small size of the study population, the small number of cases, potential misclassification of occupation at the time of death, the control of the presence or absence of other cancer risk factors, limitations of the exposure measures to general occupation, the general health status of firefighters compared to the referent population (i.e. the healthy worker effect and the inclusion of non-employed individuals in the referent group), and other study design limitations. Age is a strong predictor of prostate cancer. Most firefighter studies compare the prostate cancer incidence/mortality to a referent population incidence/mortality in a comparable age group.
- The Washington State Occupational Mortality Database, at http://www3.doh.wa.gov/OCCMORT/, for all Washington State deaths from 1950-1999 reports a PMR of 1.09 for male firefighters and prostate cancer. The result did not meet statistical significance.

[3] The upper confidence interval for Grimes et al; 1990 was truncated to allow readability of the graph OR 3.7 (95% CI 1.71- 8.02)

Prostate Cancer and Evidence for an Exposure-Response Trend:

The evidence for an exposure – response trend is presented below. Generally, studies are controlled for age of the firefighter and referent population. Age is a confounder in prostate cancer studies and is generally controlled for in the analysis phase. Race, diet and ethnicity are uncontrolled confounders in these analyses.

Table D: Prostate Cancer and Measures of Exposure-Response Relationship

Duration of Employment

Baris; 2001	**≤ 9 years**	**10 - 19 years**	**≥ 20 years**
Cases	15	5	11
SMR	**2.36 (1.42 - 3.91)**	0.47 (0.19 - 1.12)	0.72 (0.40 - 1.31)

Aronson; 1994	**< 15 years**	**15 - 29 years**	**30 + years**
Cases	1	5	9
SMR	1.61 (0.04 - 8.99)	2.43 (0.79 - 5.66)	0.97 (0.44 - 1.84)

Bates; 2001	**≤ 10 years**	**11 - 20 years**	**> 20 years**
Cases	3	1	1
SIR	1.46 (0.3 - 4.3)	0.6 (0.0 - 3.3)	0.29 (0.00 - 1.6)

Demers; 1994	**≤ 10 years**	**10 - 19 years**	**20 - 29 years**	**30 + years**
Cases	3	2	14	11
SMR	2.42 (0.5 - 7.1)	1.12 (0.1 - 4.1)	1.23 (0.7 - 2.1)	1.36 (0.7 - 2.4)

Date of Hire

Baris; 2001	**< 1935**	**1935 - 1944**	**> 1944**
Cases	12	14	5
SMR	0.75 (0.43 - 1.33)	1.36 (0.81 - 2.30)	0.83 (0.34 - 1.98)

Number of Runs

Baris; 2001	**Low (<3,323 runs)**	**Medium**	**High (≥ 5,099 runs)**
Cases	10	3	6
SMR	1.33 (0.72 - 2.48)	0.65 (0.21 - 2.03)	1.42 (0.64 - 3.16)

Time since First Employment

Guidotti; 1993	**< 20 years**	**20 - 29 years**	**30 - 39 years**	**40 - 49 years**	**50 + years**
Cases	0	1	2	2	3
SMR	xx	2.59	1.65	1.2	1.45

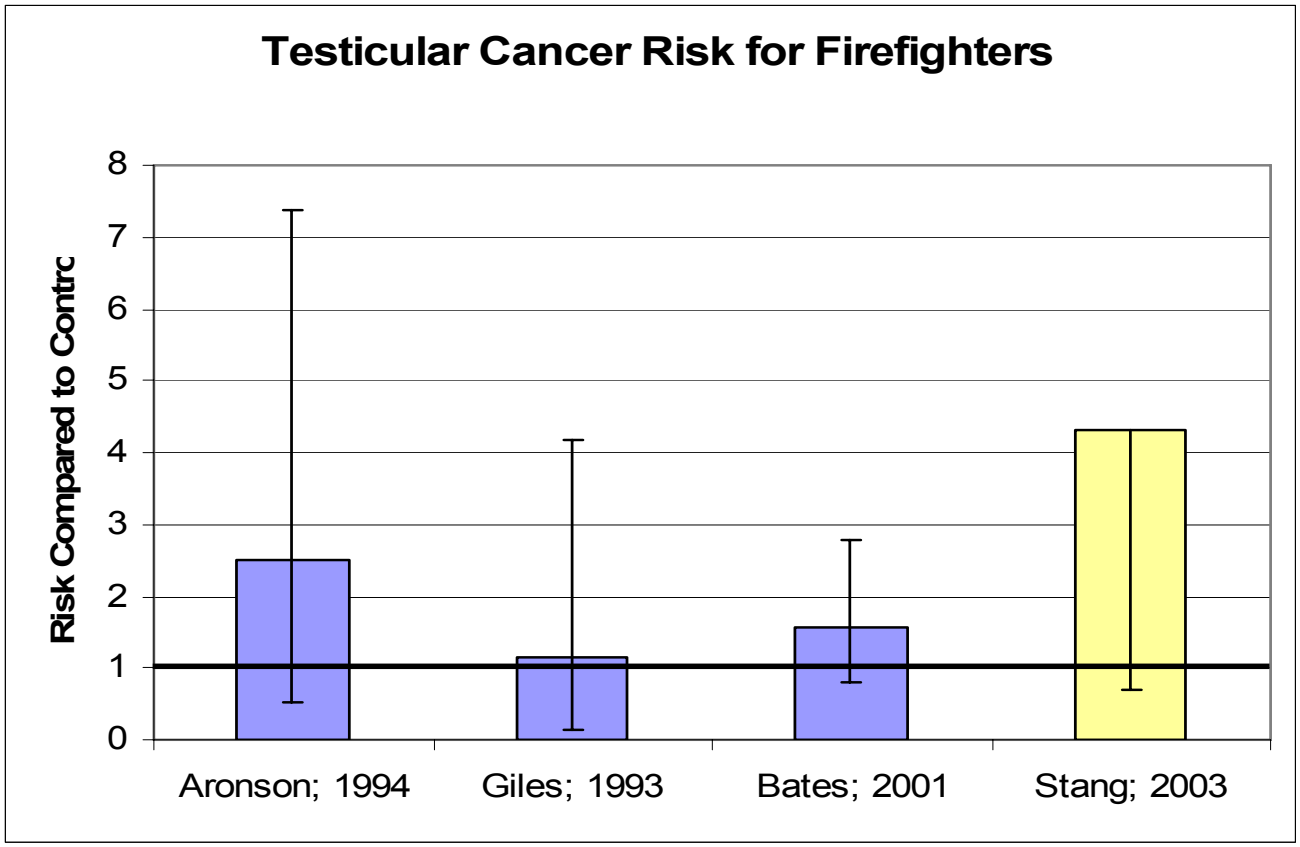
Aronson; 1994	**< 20 years**	**20 - 29 years**	**30 + years**
Cases	0	2	14
SMR	0.0 (0.0 - 16.04)	2.44 (0.3 - 8.81)	1.27 (0.69 - 2.13)

Demers; 1994	**< 20 years**	**20 - 29 years**	**30 + years**
Cases	0	0	14
SMR	0.0 (0.0 - 26.6)	0.0 (0.0 - 3.1)	**1.42 (1.0 - 2.0)**

Age of Occurrence

Demers; 1994	**18-39 years old**	**40 - 64 years old**	**≥ 65 years old**
Cases	0	4	26
SMR	0.0 (0.0 - 178)	0.86 (0.2 - 2.2)	**1.46 (1.0 - 2.1)**

Aronson; 1994	**< 60 years**	**≥ 60 years**
Cases	2	14
SMR	1.53 (0.19 - 5.52)	1.3 (0.71 - 2.18)



Purple shading are cohort studies (SMR, SIR, RR); Yellow shading are case control studies.

- Results of an association between firefighting and testicular cancer are inconsistent across studies.
- No statistically significant increased risk for testicular cancer was observed in individual studies.[4] The study by Bates when restricted to firefighters with testicular cancer developing from 1990-1996, found an elevated risk SIR 2.97 (1.3-5.9). The entire cohort from 1977 – 1996 had a SIR 1.55 (0.8-1.9) which is reported above.
- A recent study by McMasters (2006) reported a summary risk estimate from several published studies - this study uses a methodology which was not used by WA State to determine if cancers were associated with firefighting. This analysis reports the following risk estimates for testicular cancer:
  - Meta SMR – 2.50 (0.50 – 7.30)
  - Meta SIR –1.83 (1.13 – 2.79)
  - Meta Summary – 2.02 (1.30 – 3.13)
- All studies are potentially limited by one or more of the following: small size of the study population, the small number of cases, potential misclassification of occupation at the time of death, the control of the presence or absence of other cancer risk factors, limitations of the exposure measures to general occupation, the general health status of firefighters compared to the referent population (i.e. the healthy worker effect and the inclusion of non-employed individuals in the referent group, the presence or absence of testicular cancer risk factors – family history or others), and other study design limitations.
- The Washington State Occupational Mortality Database, at http://www3.doh.wa.gov/OCCMORT/, for all Washington State deaths from 1950-1999 reports a PMR of 1.10 for male firefighters and testicular cancer. The result did not meet statistical significance.

[4] The upper confidence interval for Stang et al; 1993 was truncated to allow readability of the graph - OR 4.3 (95% CI 0.7 – 30.5).

Testicular Cancer and Evidence for an Exposure-Response Trend:

The evidence for an exposure – response trend is presented below. Generally, studies are controlled for age of the firefighter and referent population. Age is a confounder in testicular cancer studies and is generally controlled for in the analysis phase.

Table E: Testicular Cancer and Measures of Exposure-Response Relationship

Duration of Employment

Bates; 2001	**≤ 10 years**	**11 - 20 years**	**> 20 years**
Cases	3	4	2
SIR	1.46 (0.3 - 4.31)	**3.51 (1.0 - 9.0)**	4.14 (0.50 - 14.9)

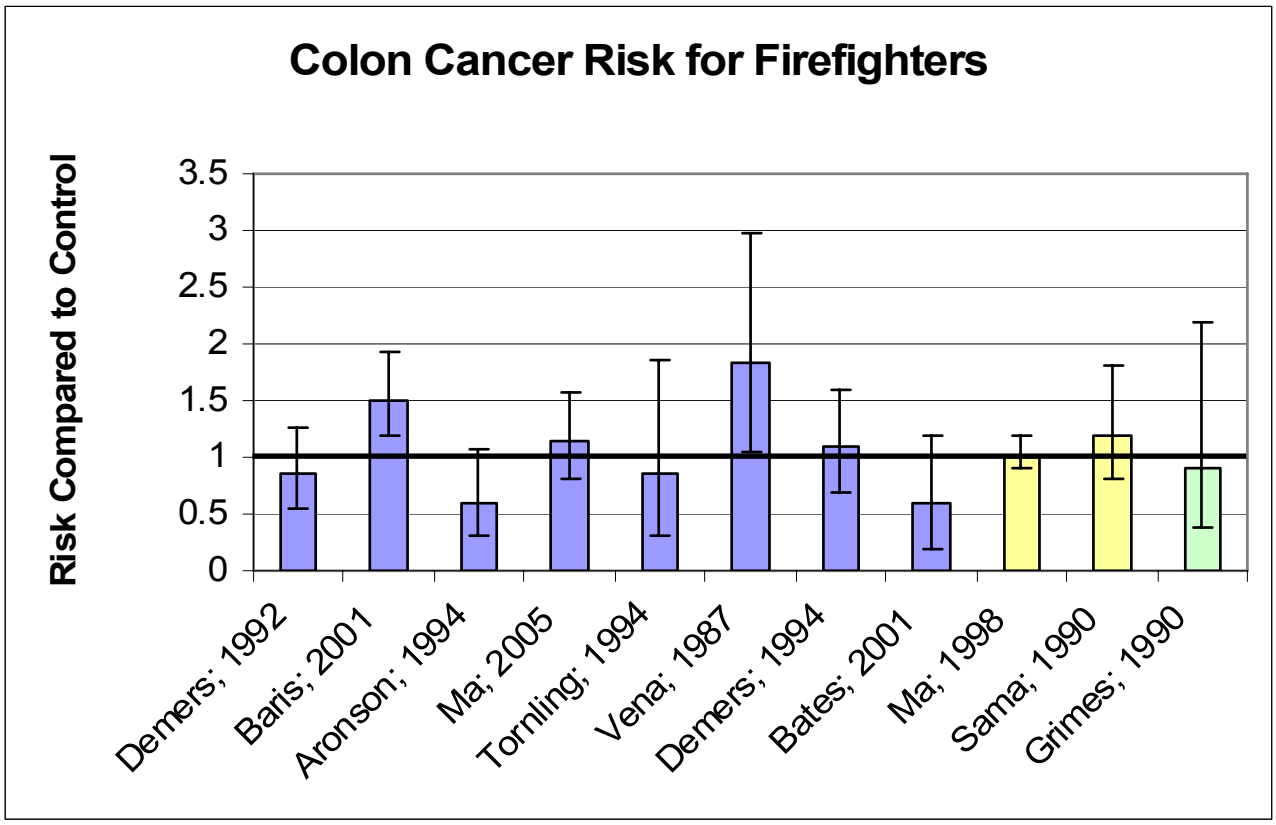
Aronson; 1994	**< 15 years**	**15 - 29 years**	**30 + years**
Cases	3	0	0
SMR	3.66 (0.75 - 10.69)	0 (0.0 - 14.19)	0.0 (0.0 - 36.89)

Time since First Employment

Aronson; 1994	**< 20 years**	**20 - 29 years**	**30 + years**
Cases	3	0	0
SMR	3.26 (0.67 - 9.53)	0 (0.0 - 24.59)	0 (0 - 30.74)

Age of Occurrence

Aronson; 1994	**< 60 years**	**≥ 60 years**
Cases	3	0
SMR	2.75 (0.57 - 8.04)	0.0 (0.0 - 40.99)



Purple shading are cohort studies (SMR, SIR, RR); Yellow shading are case control studies; Green shading are studies reporting proportionate mortality ratios (PMR).

- An association between firefighting and colon cancer is inconsistent and varies across studies.
- Two studies report a statistically significant increased risk of colon cancer in firefighters -Vena SMRs 1.83 (1.05-2.97) and Baris 1.51 (1.18-1.93).
- A recent study by McMasters GK JOEM 48(11):1189-1202 reported a summary risk estimate from several published studies - this study uses a methodology which was not used by WA State to determine if cancers were associated with firefighting. This analysis reports the following risk estimates for colon cancer:
    - Meta SMR – 1.34 (1.01 – 1.79)
    - Meta SIR –0.9 (0.69 – 1.17)
    - Meta Summary – 1.21 (1.03 – 1.41)
- Several studies measure the association between firefighting and any intestinal or colorectal cancer. (See below for summary).
- Dubrow and Wegman (1983) reported a statistically significant 'aggregate observed-expected ratio' of 1.28. The data was part of a survey of >200 occupational categories to explore occupational cancers.
- Risk factors reported by the National Cancer Institute for colon cancer include increasing age, diet, cigarette smoking, family history, and inflammatory bowel disease and other medical diseases. Other than age, these factors are not controlled in the research studies and are only relevant if the factor is either more or less present in firefighters compared to the referent population.
- All studies are potentially limited by one or more of the following: small size of the study population, the small number of cases, potential misclassification of occupation at the time of death, the control of the presence or absence of other cancer risk factors, limitations of the exposure measures to general occupation, the general health status of firefighters compared to the referent population (i.e. the healthy worker effect and the inclusion of non-employed individuals in the referent group, or others), and other study design limitations.
- The Washington State Occupational Mortality Database, at http://www3.doh.wa.gov/OCCMORT/, for all Washington State deaths from 1950-1999 reports a PMR of 0.94 for male firefighters and colon cancer. The result did not meet statistical significance. No data is available for female firefighters.

Colon Cancer and Evidence for an Exposure-Response Trend:

The evidence for an exposure – response trend is presented below. Generally, studies are controlled for age of the firefighter and referent population. Age is a confounder in colon cancer studies and is generally controlled for in the analysis phase. Diet, cigarette smoking, family history, and inflammatory bowel disease are potential uncontrolled confounders in these analyses.

Table F: Colon Cancer and Measures of Exposure-Response Relationship

Duration of Employment

Baris; 2001	**≤ 9 years**	**10 - 19 years**	**≥ 20 years**
Cases	18	16	30
SMR	1.78 (1.12 - 2.82)	1.11 (0.68 - 1.81)	**1.68 (1.17 - 2.40)**

Vena; 1987	**≤ 9 years**	**10 - 19 years**	**20 - 29 years**	**30 - 39 years**	**40 + years**
Cases	0	1	2	5	8
SMR	xx	1.25	0.87	1.43	**4.71**

Bates; 2001	**≤ 10 years**	**11 - 20 years**	**> 20 years**
Cases	1	1	5
SIR	0.41 (0.0 - 2.3)	0.46 (0.0 - 2.6)	1.37 (0.4 - 3.2)

Demers; 1992	**≤ 10 years**	**10 - 19 years**	**20 - 29 years**	**30 + years**
Cases	4	2	9	9
SMR	1.40 (0.4 - 3.6)	0.54 (0.1 - 2.0)	0.62 (0.3 - 1.2)	1.21 (0.6 - 2.3)

Date of Hire

Baris; 2001	**< 1935**	**1935 - 1944**	**> 1944**
Cases	16	28	20
SMR	1.00 (0.61 - 1.63)	**2.00 (1.38 - 2.90)**	**1.60 (1.03 - 2.49)**

Vena; 1987	**< 1930**	**1930 - 1939**	**1940 - 1949**	**1950+**
Cases	10	4	2	0
SMR	**2.27**	**2.35**	1.11	0

Number of Runs

Baris; 2001	**Low (<3,323 runs)**	**Medium**	**High (≥ 5,099 runs)**
Cases	23	16	9
SMR	**1.93 (1.29 - 2.91)**	**2.22 (1.36 - 3.62)**	1.22 (0.64 - 2.35)

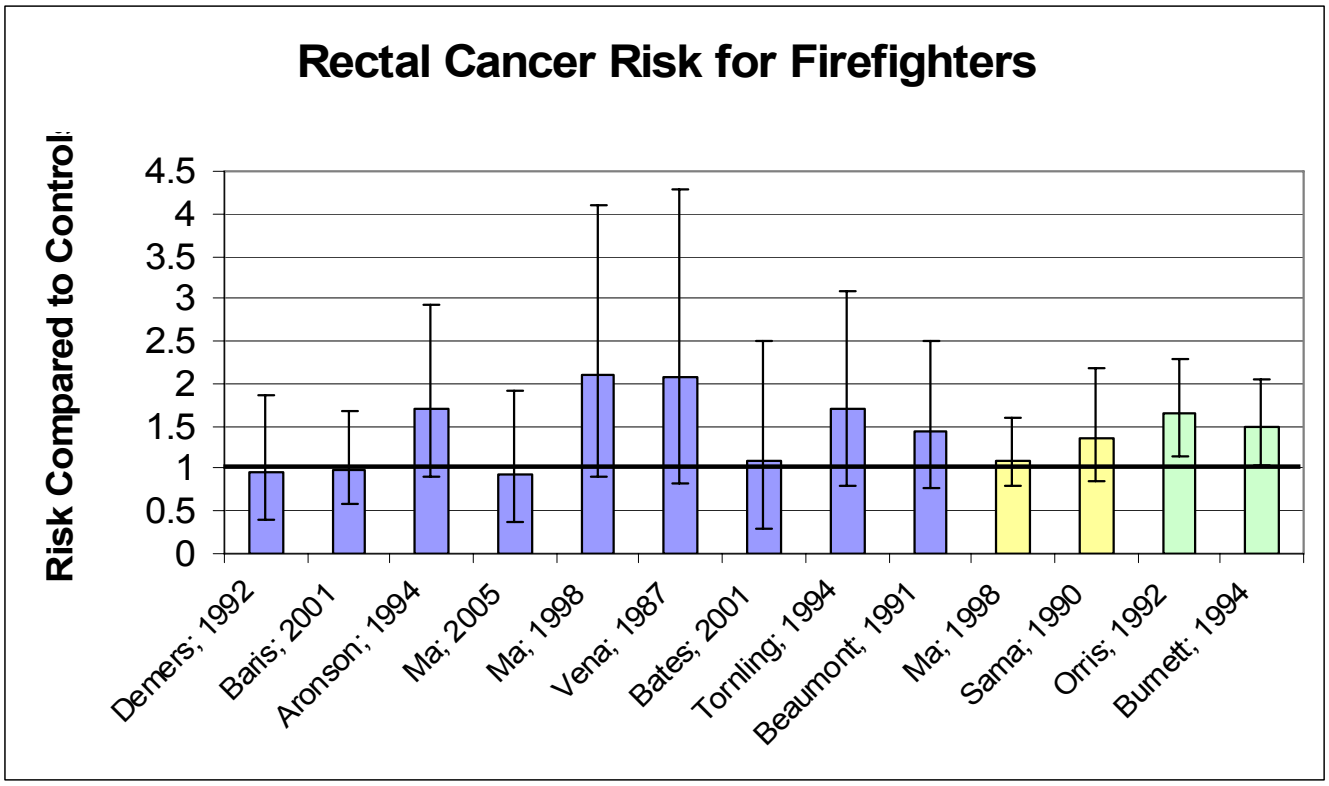
Time since First Employment

Vena; 1987	**< 20 years**	**20 - 29 years**	**30 - 39 years**	**40 - 49 years**	**50 + years**
Cases	0	2	4	7	3
SMR	xx	1.3	1.51	**2.65**	**2.85**

Demers; 1992	**< 20 years**	**20 - 29 years**	**30 + years**
Cases	1	3	20
SMR	0.51 (0.1 - 2.9)	0.66 (0.1 - 1.9)	0.91 (0.6 - 1.4)

Age of Occurrence

Demers; 1992	**18-39 years old**	**40 - 64 years old**	**≥ 65 years old**
Cases	1	10	13
SMR	1.38 (0.1 - 8.2)	0.78 (0.4 - 1.4)	0.86 (0.5 - 1.5)



Purple shading are cohort studies (SMR, SIR, RR); Yellow shading are case control studies; Green shading are studies reporting proportionate mortality ratios (PMR).

- Results of an association between firefighting and rectal cancer are inconsistent. There are multiple studies with point estimates approaching statistical significance to the level of 1.5-2.0 times increased risk.
- A statistically significant increased risk of rectal cancer was reported in two studies - Burnett PMR 1.48 (1.05 – 2.05) and Orris PMR 1.64 (1.14 – 2.30).
- A recent study by McMasters (2006) reported a summary risk estimate from several published studies - this study uses a methodology which was not used by WA State to determine if cancers were associated with firefighting. This analysis reports the following risk estimates for rectal cancer:
    - Meta SMR – 1.33 (1.00 – 1.73)
    - Meta SIR –1.14 (0.81 – 1.54)
    - Meta Summary – 1.29 (1.10 – 1.51)
- All studies are potentially limited by one or more of the following: small size of the study population, the small number of cases, potential misclassification of occupation at the time of death, the control of the presence or absence of other cancer risk factors, limitations of the exposure measures to general occupation, the general health status of firefighters compared to the referent population (i.e. the healthy worker effect, the inclusion of non-employed individuals in the referent group, the presence or absence of colorectal cancer risk factors – family history, high fat diet, or others), and other study design limitations.
- The Washington State Occupational Mortality Database, at http://www3.doh.wa.gov/OCCMORT/, for all Washington State deaths from 1950-1999 reports a PMR of 1.05 for male firefighters and rectal cancer. The result did not meet statistical significance. No data is available for female firefighters.

Rectal Cancer and Evidence for an Exposure-Response Trend:

The evidence for an exposure – response trend is presented below.

Table G: Rectal Cancer and Measures of Exposure-Response Relationship

Duration of Employment

Baris; 2001	**≤ 9 years**	**10 - 19 years**	**≥ 20 years**
Cases	3	6	5
SMR	0.86 (0.28 - 2.66)	1.16 (0.52 - 2.58)	0.92 (0.38 - 2.22)

Aronson; 1994	**< 15 years**	**15 - 29 years**	**30 + years**
Cases	0	5	8
SMR	0 (0.00 - 4.67)	2.35 (0.76 - 5.48)	1.74 (0.75 - 3.43)

Bates; 2001	**≤ 10 years**	**11 - 20 years**	**> 20 years**
Cases	2	2	4
SIR	1.22 (0.1 - 4.4)	1.38 (0.2 - 5.0)	1.61 (0.4 - 4.1)

Beaumont; 1991	**3 - 9 years**	**10 - 19 years**	**20 - 29 years**	**30 + years**
Cases	0	2	6	5
RR	0	2.19	1.45	1.42

Demers; 1994	**≤ 10 years**	**10 - 19 years**	**20 - 29 years**	**30 + years**
Cases	2	3	5	2
SIR	1.4 (0.2 - 4.9)	1.9 (0.4 - 5.4)	0.7 (0.2 - 1.6)	1.6 (0.2 - 5.6)

Date of Hire

Baris; 2001	**< 1935**	**1935 - 1944**	**> 1944**
Cases	7	3	4
SMR	1.05 (0.50 - 2.21)	0.73 (0.23 - 2.26)	1.20 (0.45 - 3.20)

Number of Runs

Baris; 2001	**Low (<3,323 runs)**	**Medium**	**High (≥ 5,099 runs)**
Cases	5	1	1
SMR	1.37 (0.51 - 3.29)	0.51 (0.07 - 3.59)	0.54 (0.08 - 3.85)

Time since First Employment

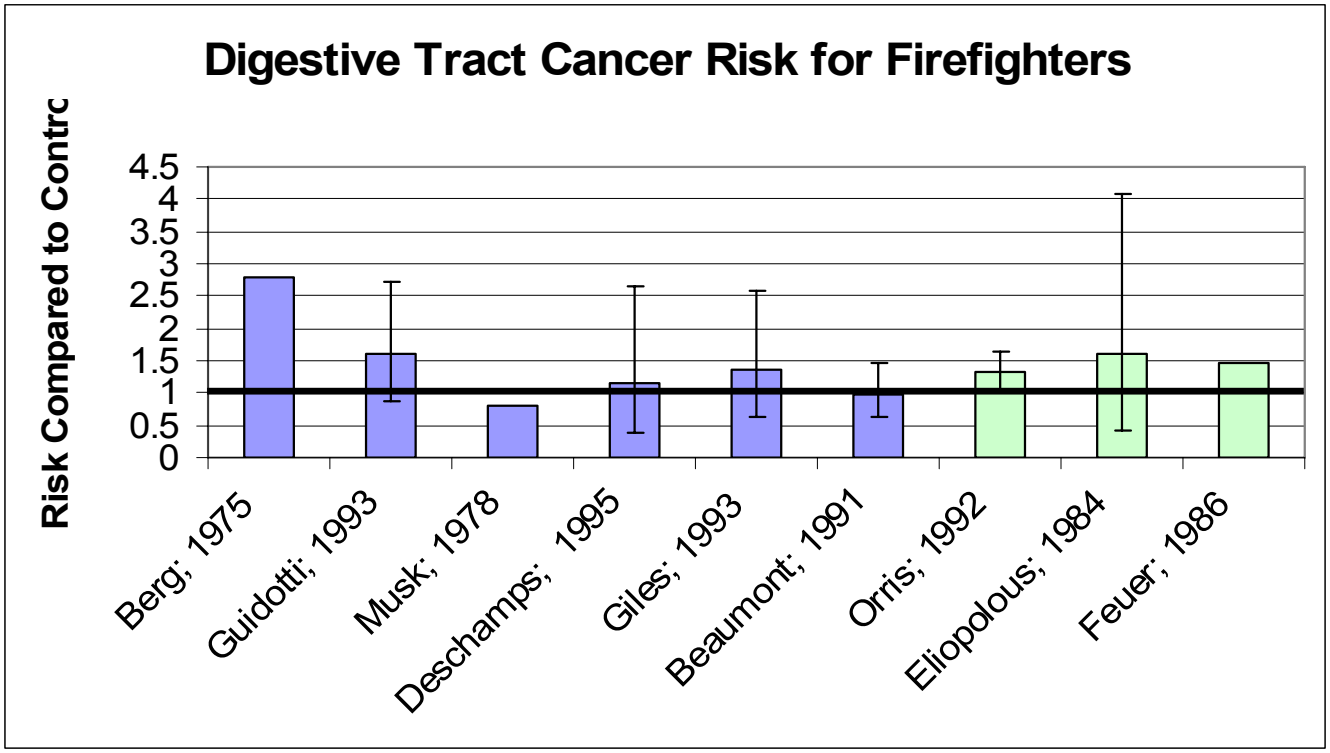
Beaumont; 1991	**3 - 19 years**	**20 - 29 years**	**30 - 39 years**	**40 + years**
Cases	2	2	3	6
RR	2.64	1.05	1.04	1.77

Aronson; 1994	**< 15 years**	**15 - 29 years**	**30 + years**
Cases	1	2	10
SMR	1.34 (0.034 - 7.53)	1.46 (0.18 - 5.27)	1.82 (0.87 - 3.36)

Demers; 1994	**< 20 years**	**20 - 29 years**	**30 + years**
Cases	0	4	8
SMR	0.0 (0.0 - 8.8)	2.2 (0.6 - 5.7)	0.8 (0.4 - 1.7)

Age of Occurrence

Burnett; 1994	**< 65 years**
Cases	18
PMR	**1.86 (1.10 - 2.94)**



Purple shading are cohort studies (SMR, SIR, RR); Green shading are studies reporting proportionate mortality ratios (PMR).

- Additional studies for digestive cancers likely include cancers of the colon, rectum and other organs in the gastrointestinal tract. The descriptions of the cancers included in these studies are Digestive (Musk, Deschamps and Feuer), Colorectal (Berg, Guidotti, and Giles), Intestinal (Eliopolous, Orris) and Intestinal except Rectum (Beaumont).
- The study by Berg reported a statistically significant increased risk of colorectal cancer SMR – 2.79.
- The study by Orris reported a statistically significant increased risk of intestinal cancer SMR – 1.31 (1.04-1.65).

Digestive Cancer Studies and Evidence for an Exposure-Response Trend:

The evidence for an exposure – response trend is presented below.

Table H: Other Digestive Cancers and Measures of Exposure-Response Relationship

Duration of Employment

Feuer; 1986	≤ 20 years	11 - 20 years	> 20 years
Cases	5	5	10
PMR	1.24	0.96	1.15

Beaumont; 1991	3 - 9 years	10 - 19 years	20 - 29 years	30 + years
Cases	1	4	7	12
RR	0.92	1.67	0.64	1.22

Time since First Employment

Beaumont; 1991	3 - 19 years	20 - 29 years	30 - 39 years	40 + years
Cases	4	2	8	10
RR	2.27	0.45	1.06	0.94

Feuer; 1986	≤ 22 years	22 - 27 years	>27 years
Cases	4	7	9
PMR	0.92	1.28	1.1

Guidotti: 1994	< 20 years	20 - 29 years	30 - 39 years	40 - 49 years	50+ years
Cases	2	5	3	2	2
SMR	1.48	2.68	1.24	1.2	1.46

Age of Occurrence

Giles; 1993	≥ 65 years
Cases	6
SIR	**3.65 (1.13 - 7.94)**

Discussion:
Workers' compensation laws for presumptive coverage of cancer in firefighters vary considerably across the US states and the Canadian provinces.[5,6] Many states have laws which identify specific cancer types presumed to be related to the firefighting occupation, while some states do not have presumptive coverage for any cancer. A likely explanation for the state-to-state variability is the blending of public policy goals with the epidemiologic research suggesting causality between selected cancers and firefighting.

Generally, epidemiologic research would support an occupational cause for a disease, if the following criteria were satisfied:[7]

- The chemical, physical and biologic exposure precedes the disease;
- The association between the exposed population and the disease or injury outcome is of a sufficient magnitude to support an individual presumption. The stronger the association the more likely it is that its relation is causal. Typically, the estimate of increase occupational risk is more than twice the expected risk of the control population. This estimate allows the presumption to apply to any one individual;
- The association is consistent across a number of studies in different populations and study designs. Evidence of an association may occur due to statistical chance in any one study, whereas this is reduced if there are multiple studies demonstrating a statistically significant increased risk;
- There is biologic plausibility that the chemical, physical, or biological occupational exposures are associated with the disease. The research studies would have to allow some estimation of, or actual measurement of the suspected occupational exposures in the individuals under study and in the control population to which they are being compared;
- That there is a dose-response relationship, such that an increasing amount of exposure increases the risk.
- Elimination or control of alternative explanations for the potential relationship between the disease and the occupation. In other words, if an additional factor is related to both the exposure and the disease, then it should be accounted for either in the study design or analysis.
- The association is compatible with the existing theory or knowledge.

In reviewing the above epidemiologic research criteria, to support presumption based on a review of the scientific literature, one would optimally like many high quality research studies, which control for bias, chance and confounders, which demonstrate a strong consistent dose response effect of firefighting to a cancer. The causation of that cancer would be consistent with known firefighting exposures to known carcinogens.

However, almost all scientific research is subject to criticism regarding the study design and limitations of the research findings. Studies looking for an association between cancer incidence/mortality and firefighters are no exception. Almost all firefighter studies are retrospective cohort studies or case control studies which do not account for potential differences between firefighters and the reference population regarding alternative causes or risks of cancer. For example, firefighters may be in better physical condition and more healthy than the comparison population, a 'healthy worker' thus blunting an association or there may be differences in the diet of a firefighter to a referent population, e.g. a high fat, low fiber diet is associated with colorectal cancer. The duration of follow-up for firefighters, the misclassification of disease and exposure may underestimate the number of cases attributable to firefighters and firefighting and suggest a negative association when in fact one exists. There are few, if any, exposure assessment on an individual level.

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[5] The statutory presumption shifts both the burden of production and the burden of persuasion to the party claiming that the disability is not work-related. Evidence that a disability is not caused by work is insufficient to rebut the presumption; the evidence must show that the disability was more probably than not caused by a non-work-related cause and identify the cause.

[6] A review of the firefighter presumptive coverage laws across US states and Canadian Provinces is available from the International Association of Firefighters (http://www.iaff.org/safe/content/presumptive/Presumptive_Laws.htm). For example, California and Texas cover all cancers if there is exposure to a known carcinogen related to the individual cancer type. Oregon, Michigan and Idaho do not have firefighter presumptive coverage laws for cancer. New York specifies a list of cancers - digestive, hematological, urinary, neurological, breast, reproductive, or prostate systems which would be covered.

[7] Hills Criteria of Causation outlines the minimal conditions needed to establish a causal relationship between two items.

There are some general limitations of the firefighter studies that should be considered when individual studies are applied to the entire firefighter population, either throughout Washington State or nationally. In general, research studies regarding cancer incidence or mortality are performed in urban populations with career firefighters. Almost all studies are focused on male firefighters and thus information on the health risks to female firefighters is poorly understood. There are several studies that overlap in both the geographic area studied and the largest population cohort analyzed is included in the summaries. The studies are from a diverse number of countries and US municipalities. Exposure conditions for firefighters likely differ among countries, because of differing firefighting techniques. Additionally, exposure conditions likely vary due to the time period captured in the populations under study. Building materials and their combustion products likely differ from the pre- and post- WW II eras. The use of asbestos, plastic building materials, and other construction materials has changed over time likely affecting the mix of potential carcinogens present.

Given the limitations of the scientific studies, there is a level of scientific uncertainty associated with determining the association between firefighting and occupational cancers. Yet, this scientific uncertainty intersects with and must be considered in relation to the public policy goals of developing firefighter presumption laws.

The public policy goals for firefighter presumption laws likely reflect:

- An appreciation of the personal risk and sacrifice of public safety personnel,
- A recognition of the unique nature of work as a firefighter with regards to uncontrolled exposures to chemical, biological and physical hazards including known and unknown carcinogens, and
- That in order to avoid serious or irreversible potential harm to firefighters, despite lack of scientific certainty as to the likelihood, magnitude, or causation of that harm, that protective public policy measures may be warranted.

Blending both the public policy goals with the epidemiologic research studies related to firefighters and cancer is difficult and subject to individual interpretation. Ultimately, the Washington State legislature will have to determine which cancers qualify for presumption in firefighters.

A Brief History of Firefighter Presumption in Washington State

Washington State is one of many states with firefighter presumption laws. The first benefit for presumption was in 1987, when presumption was granted for firefighters with respiratory disease (RCW 51.32.185).

In 2001, with the introduction of an expanded firefighter presumption statute to include all cancers, the primary review of the peer-reviewed literature for cancer presumption was based on the combination of the following three criteria:

- there was a statistically significant increased association between firefighting and cancer,
- the association demonstrated that firefighters had twice the risk of the reference population, and
- the findings were consistent across at least three independent studies.

The 2001 legislation was not passed.

In 2002, after the events of September 11, 2001, there was a renewed public policy attention to the personal risk firefighters encounter on the job. On review of the existing literature, the cancers where there were multiple studies demonstrating a statistically significant increased risk to firefighters of at least 1.5 times that of the referent were included in legislation. The rationale for lowering the threshold from twice the risk was the suspicion that firefighters likely were a healthier population than the referent controls and as well were exposed to significant levels of known and unknown carcinogens. A rationale for this approach is guided by regulatory policy where a decision 'may be fully supportable if it is based on the inconclusive but suggestive results of numerous studies. By its nature, scientific evidence is cumulative: the more supporting, albeit inconclusive

evidence available, the more likely the accuracy of the conclusion.'[8] Cancers included into RCW 51.32.185 were primary brain cancer, leukemia, non-Hodgkins lymphoma, kidney, ureter, bladder, and melanoma.

In 2007, the legislature is considering expanding the presumption to include stomach, intestinal (colon/rectal), prostate, testicular, and multiple myeloma.

Criterion Used by Other Workers' Compensation Boards

In 1994, the Industrial Disease Standards Panel of the Ontario Workers' Compensation Board reviewed the association between the firefighter occupation and selected cancers (IDSP, 1994; Guidotti, 2003). The internal criteria used were:

- An SMR that is statistically significant,
- An SMR that achieves a level of 170 (1.7x) whether or not it is statistically significant,
- A lower end of the 95% confidence interval that falls between 90 and 100, and
- A dose-response relationship or evidence from other sources and jurisdictions.

An independent analysis by Guidotti (1995) using different criterion was published and widely cited as a rationale approach to the relationship of selected cancers and firefighting. The criterion blended expert opinion mixed with the epidemiologic criterion for causality plus an evaluation of the strengths and weakness of the individual studies.[9] His approach was similar to the Institute of Medicine's committee's approach assessing the role of Agent Orange on human health -

> The evaluation of evidence to reach conclusions about statistical associations goes beyond quantitative procedures at several stages: assessing the relevance and validity of individual reports; deciding on the possible influence of error, bias, confounding, or chance on the reported results; integrating the overall evidence within and between diverse fields of research; and formulating the conclusions themselves.

Guidotti updated his work in 2003 as a rationale for Canadian provincial legislation for firefighter cancer presumption (Guidotti, 2003). The approach by IDSP and Guidotti derived a list of cancers similar to Washington's existing firefighting presumption – kidney, ureter, bladder, primary brain cancer, leukemia, and non-Hodgkin's lymphoma.[10]

Summary of Epidemiologic Research Data for Selected Cancers for Firefighter Presumption

In reviewing the information in the summary of cancer studies (above), we can consider some of the epidemiologic criteria that may be helpful in influencing the public policy decision of which cancers to include in the presumption. In 2002, the 'criteria' used in Washington State were based on having multiple studies demonstrating a statistically significant increased association with firefighting. By having multiple statistically significant studies which demonstrate a positive association, it excludes the possible spurious result obtained from one study, a 'false positive,' and can demonstrate some level of consistency across studies. In 2002, we did not consider whether there was an exposure response relationship between firefighting duration of employment and cancer. Information on the dose response can support qualification for presumption and is considered further in this review.

Intestinal - Colon: Of the 11 independent colon cancer studies in this review, there are two studies which estimated a statistically significant increased risk of colon cancer in firefighter cohorts of $\geq$1.5 times the referent

[8] DC Circuit Court ethylene oxide decision, Public Citizen v Tyson, 1986.

[9] A more formalized evaluative process for reviewing individual studies has been developed by the American Academy of Neurology. See Edlund W, Gronseth G, So Y, Franklin G. (2004) Clinical Practice Guideline Process Manual, 2004 Ed., American Academy of Neurology. St. Paul MN. Available at http://www.aan.com/professionals/practice/pdfs/2004_Guideline_Process.pdf.

[10] Washington includes malignant melanoma whereas this cancer is not included in Canadian legislation.

population (Vena, 1987; Baris, 2001). A third study by Berg (1975) reviewing colon and rectal cancer reported an increased risk of 2.79. Two study cohorts demonstrated an increased association of colon cancer due to duration of employment (Vena, 1987; Baris, 2001). Generally, the studies do not control for confounders such as diet, family history, inflammatory bowel disease and smoking. Whether controlling these factors would influence the result is unknown.

Despite the limitations of the research studies and considering the additional evidence associated with an exposure response relationship, the epidemiologic evidence approximates the criteria used in 2002 to support a presumption in firefighters for colon cancer.[11]

Intestinal – Rectal: Of the 13 independent rectal cancer studies in this review, there are two studies which estimated a statistically significant increased risk of rectal cancer in firefighter cohorts of ≥1.5 times the referent population (Orris, 1992; Burnett, 1994). Both of these studies have a weaker study design, reporting a PMR, than the other studies noted. A third study by Berg (1975) reviewing colon and rectal cancer reported a statistically significant increased risk of 2.79 times control. No study demonstrated an increased association of rectal cancer due to duration of employment. Two epidemiologic cohort studies approached statistical significance (95% Lower CI ≥ 0.9) and had an estimate of ≥ 1.5 times the risk. Generally, the studies do not control for confounders such as diet, family history, inflammatory bowel disease and smoking.

Despite the limitations of the research studies and considering the studies approaching statistical significance but limited due to sample size, the epidemiologic evidence approximates the criteria used in 2002 to support a presumption in firefighters for rectal cancer.

Multiple Myeloma: Of the 6 independent multiple myeloma cancer studies reviewed, there was only one study demonstrating a statistically significant increased risk of multiple myeloma in a firefighter cohort from 27 states of ~1.5 times the referent population (Burnett, 1994). This study has a weaker study design, reporting a PMR, than the other studies noted but has the advantage of a large number of observed cases. The study by Baris reported a result approaching statistical significance (lower 95% CI ≥0.90) with an estimate of increased risk at 1.68 times the referent population. This same study reported an statistically significant exposure response trend. Firefighters with ≥ 20 years of employment as a firefighter had a statistically significant increased risk of ≥1.5 times the risk of the comparison population.

Two additional studies, which aggregate data across studies, suggest a statistically significant increased risk for firefighters for multiple myeloma of ≥ 1.5 times the control population (Dubrow, 1983; LeMasters, 2006). These studies combine data sources to estimate risk in firefighters. If the lists of cancers potentially eligible for presumption are derived from such studies – the suggestion might be to adopt the entire methodology for determining cancer presumption. This is not a recommended approach given that some individual studies may have sufficient number of cancer cases to estimate an increased or decreased risk. Nevertheless, these studies do provide information that may be considered valuable by public policy makers and researchers. The primary advantage of combining cases is to overcome the small number of observed cases in the study population. Multiple myeloma has the lowest incidence rate of the selected cancers (Table A). Additionally the evidence may be viewed in the light of the absence of known alternative risk factors that would significantly bias the result towards a positive association.

The evidence from research studies supporting a positive association between firefighters and multiple myeloma is inconsistent with the criteria used in 2002 to support a presumption in firefighters for multiple myeloma. Some supportive evidence of an association between multiple myeloma and the firefighting occupation is derived from the studies described above.

[11] A rationale for Canadian legislation for firefighter presumption for cancer (Guidotti, 2003) supports the inclusion of colorectal cancer.

Testicular Cancer: Of the 4 independent testicular cancer studies reviewed, none demonstrated a statistically significant increased testicular cancer risk in firefighters of ≥ 1.5 times the risk of the referent population. The study by Bates when restricted to firefighters with testicular cancer developing from 1990-1996, found an elevated incidence of 2.97 times the comparison population. The entire cohort from 1977 – 1996 had a non-significant elevated risk of 1.55 times the comparison population. No studies reported a result approaching statistical significance (lower 95% CI 0.90) with a risk estimate ≥ 1.5.

One additional study, which aggregates data across studies, suggests a statistically significant increased incidence of testicular cancer in firefighters at ≥ 1.5 times the incidence of the control population (LeMasters, 2006). The summary risk estimate was statistically significant and > 2.0 times the risk. The primary advantage of combining cases is to overcome the small number of observed cases in the study population. Testicular cancer has a low incidence rate (Table A). There are a couple of known alternative risk factors that could influence the result (e.g. cryptorchidism and family history) however these risk factors would be readily apparent for a rebuttal of the presumption.

The quantity of the available research studying the association between firefighters and testicular cancers is insufficient to meet the 2002 criteria. There is supportive evidence of a positive association between testicular cancer and the firefighting occupation but it relies on the aggregation of studies and restriction to subgroups of firefighters. Additional evidence is likely needed for a more complete assessment.

Stomach Cancer: Of the 14 independent stomach cancer studies reviewed, there was only one study demonstrating a statistically significant increased risk of stomach cancer in a firefighter cohort. Swedish firefighters had a 1.9 times increased risk of cancer compared to the referent population (Tornling, 1994). The same study reported an exposure response trend with firefighters with ≥ 30 years of employment as a firefighter. One additional cohort from San Francisco reported a statistically significant increased risk ≥ 1.5 times the referent population for firefighters with ≥ 40 years since first employment. No studies reported a result approaching statistical significance (lower 95% CI 0.90).

One additional study, which aggregates data across studies, suggest a statistically significant increased risk for firefighters for stomach cancer of ≥ 1.5 times the control population (LeMasters, 2006). The primary advantage of combining cases is to overcome the small number of observed cases in the study population. Stomach cancer has a low incidence rate of the selected cancers (Table A). There are a few known alternative risk factors may influence the result, including diet, and smoking status.

The evidence from research studies supporting a positive association between firefighters and stomach cancer is inconsistent with the criteria used in 2002 to support a presumption in firefighters for stomach cancer. Given the large number of studies, there is minimal supportive evidence of an association between stomach cancer and the firefighting occupation.

Prostate Cancer: Of the 15 independent prostate cancer studies reviewed, there was only one study of Honolulu firefighters demonstrated a statistically significant increased risk of prostate cancer (Grimes, 1990). This study had a weaker study design, reporting a PMR, than the other studies noted. However, one study demonstrated a 60% reduction in the risk of prostate cancer in San Francisco firefighters (Beaumont, 1991). The risk in Honolulu firefighters was 3.7 times the Hawaiian comparison population. No cohorts demonstrated a meaningful exposure response trend. No studies reported a result approaching statistical significance (lower 95% CI 0.90) with a risk estimate ≥ 1.5. See section above which report results for estimated risk ≤ 1.5.

Race is a known alternative risk factor for prostate cancer, which may influence the result. African Americans have higher rates and Asian Americans have lower rates when compared to Caucasian populations. The

Hawaiian study does not define the demographics and race characteristics of the study population or the referent population for a determination of the influence of race on the estimates of risk.

The evidence from research studies supporting a positive association between firefighters and prostate cancer is inconsistent with the criteria used in 2002 to support a presumption in firefighters for prostate cancer. Conflicting evidence of any meaningful association between prostate cancer and the firefighting occupation is derived from the studies described above.

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