Cancer Among Firefighters in 2004:
Interpreting the Evidence

A Report to the British Columbia Professional Fire Fighters Association

Tee L. Guidotti
Division of Occupational Medicine and Toxicology
Dept. of Medicine
School of Medicine and Health Sciences
The George Washington University Medical Center
2100 M St., NW, Ste. 203
Washington DC 20037
Tel.: 202 994-1765
Fax: 202 994-0011
eohtlg@gwumc.edu

15 September 2004

Executive Summary

There has been a movement across Canada to adopt legislation establishing rebuttable presumptions for compensation of firefighters who develop certain types of cancer. Such presumptions must meet legal standards of the weight of evidence.

The Workers' Compensation Board of British Columbia commissioned a report in 2003 from a team of consultants associated with Cancer Care Ontario. The team members were charged with evaluating the extant data on risk of occupational cancer among firefighters; the report, which is based on a rather stereotyped model of meta-analysis, has limited utility. Notwithstanding the stated objectives of the study (which changed in sequential drafts of the reports), the assessment is based on strength of evidence, not weight of evidence, which is fundamental to adjudication for compensation. The Cancer Care Ontario team also omitted useful studies and restricted their analysis to summary risk estimates rather than examining all pertinent data, contrary to their (final set of) stated objectives. The study report is examined in detail.

In the present report, the epidemiological data are examined with careful attention to sources of bias and misclassification (which, in general, tend to produce underestimates of risk) and individual studies are reviewed for the information they may yield. This assessment is an update and elaboration of our previous analyses, which have been peer-reviewed and presented for open discussion in professional venues.

The presumptions for bladder cancer and kidney cancer are grounded on substantial evidence that already meet scientific standards of certainty. The presumption for testicular cancer is based on an emerging literature suggesting a high risk but illustrate the "first case" problem: the first case of a previously unrecognized work-related condition to come to adjudication is likely to be denied because the literature does not exist to support it. The presumptions for brain cancer, non-Hodgkin lymphomas and leukemias are based on the inference that within the overall category there are specific disorders for which the evidence suggests an elevated risk but it is not possible to discern which are in excess. The argument for a presumption for nonsmoking firefighters with lung cancer may also apply in some cases to colon cancer. These issues illustrate approaches to applying epidemiological data to these problems in the individual case or

claim, where scientific standards of certainty do not apply and the legal requirement is a determination on the basis of the weight of evidence.

Table of Contents

Executive Summary	2
Introduction	5
Background to this Analysis	6
Critique of the Cancer Care Ontario Report *Characteristics of the team* *The report* *Findings for cancer at specific sites* *The supplement*	7
The Rationale of Adjudication	19
The Evidentiary Base	21
Genitourinary Cancers: The "normal" case *Kidney cancer* *Testicular cancer*	26
Brain: Many diseases in which one group predominates	28
Leukemia, Lymphoma, Myeloma: Many individual diseases in which no one disease predominates *Non-Hodgkin's Lymphomas* *Leukemias* *Myeloma* *Interpretation*	30
Lung Cancer *Lung Cancer* *What is the Unconfounded Risk Attributable to Fire fighting?* *The Non-Smoking Fire fighter*	34
Other Tumour Sites	39
Evaluation in Light of Recent Evidence	40
Table 1: Comparison of Conclusions	42
Bibliography	43

Introduction

The occupational health problems of firefighters have been extensively studied, to the point that the world epidemiological literature on this topic is among the most complete and detailed available for any occupation. Even so, many unresolved issues remain, especially whether firefighters are at increased risk for certain cancers.

Firefighters may be at risk for a number of exposure-related cancers because of their occupational exposure to a variety of toxic agents.[1] A major unproven hypothesis is that risk increased following the introduction in the 1950's of combustible plastic furnishing and building materials known to generate toxic combustion products which may be carcinogenic.[2] However, the evidence for excess of certain cancers has been equivocal. This has led to great controversy and inconsistency in the adjudication of claims for occupational disease.

Although recent findings have led to an appreciation of the risk for one new outcome, testicular cancer, as will be discussed below, most of these issues are unlikely to be resolved by more data.[3] Most large studies on firefighters are similar in design and face similar limitations on power for rare outcomes. Meta-analysis has therefore been applied to the literature on firefighters, with mixed results in light of subsequent studies.[4] The method confirmed elevations for some cancers (brain and myeloma) that were already recognized but does not address the issues that will be raised later in this paper. Pooled studies with large populations have not fully resolved these issues, either.[5]

We suggest that these issues represent a class of problem in occupational epidemiology that is best approached outcome by outcome using principles of logic rather than advanced statistical techniques or meta-analysis.[6] Key to the validity of the methods described in this paper is the essential criterion that it is the weight of evidence, not scientific certainty, that determines the outcome of the case or claim in a legal setting, such as tort litigation and adjudication for compensation benefits.

In this report the ethical and public policy arguments for providing public safety workers with special consideration will not be discussed in detail but underlie the movement in Canada to legislate presumptions. As a matter of social policy, it may be justified to provide public safety workers with additional protection. Canadian legislators have said (for example, in radio interviews)

that presumptions giving the benefit of the doubt to firefighters are justified because firefighters are subjected to an occupational risk that would be intolerable in other lines of work and have done so because of overriding public interest. The role of the expert is not to argue public policy but to provide a basis for its equitable implementation.

Background to this Analysis

In 2002, a movement arose in Canada to re-examine compensation for firefighters who develop certain cancers suspected to be work-related. The movement began with the provincial government of Manitoba, which enacted legislation for presumption for various cancer outcomes in 2002. By April 2003, bills had been passed by the provincial legislatures in Alberta, Nova Scotia and Saskatchewan and had been introduced in New Brunswick. Ontario had previously dealt with the issue by adopting the recommendations as policy for the WCB. British Columbia committed itself to a review of the evidence, which will be discussed in greater detail below. The speed of this legislative movement is almost unprecedented in Canadian workers' compensation.

In 2002, when the issue first became a topic of legislative interest, we were asked to prepare a report on the health risks to firefighters for the Government of Manitoba. A scientific paper based on this report was peer reviewed and published in 2003. We have subsequently advised the Government of Manitoba on plans to follow up on their policies with epidemiological surveillance to determine the actual experience of firefighters in the province in coming years. [7]

Subsequently, we were asked to prepare a more detailed report by the British Columbia Professional Fire Fighters Association (BCPFFA) on similar issues. This guidance was intended to support proposals for the amendment of the provincial Workers' Compensation Acts with respect to establishing presumption for occupational disease among firefighters.

In 2003, the Workers' Compensation Board of British Columbia contracted with the Division of Preventive Oncology of Cancer Care Ontario to conduct an assessment of the literature on firefighting and cancer risk. This agency is well regarded for its expertise on cancer epidemiology in general and, in the past, has featured such well-known epidemiologists on its staff as Geoffrey Howe. This report was completed on February 2004 and sent for peer review. In March 2004, an addendum to the report was issued, reversing some of the conclusions. The Cancer Care Ontario report has not been published in the open literature. It is the understanding

of the author of the present report that the investigators from Cancer Care Ontario were screened to select investigators who had not previously studied firefighters. The team members were not given access to prior reports or permission to review our previous reports and publications, on the grounds that they were mandated only to evaluate the unvarnished evidence and that a review of the total literature might introduce bias.

The BCPFFA requested that the author review the report form the Cancer Care Ontario team and comment on it. This is the response to that request.

Critique of the Cancer Care Ontario Report

We have received, through the BCPFFA, the document entitled "The Occupation of Firefighting and Cancer Risk: Assessment of the Literature: Report to the Workers[']Compensation Board of British Columbia", dated 15 June 2004 and the penultimate draft dated February 2004 which was circulated to reviewers and which was labeled "Working Final Draft: Subject to Revision Following Review". We also received the "Addendum to the Final Working Draft", dated March 2004. All three documents have been reviewed.

Characteristics of the team

In order to determine the backgrounds of the authors and to confirm that they had not previously been engaged in studies on firefighters, we conducted a Medline search on each. Those with PhD degrees we assume to be the principal investigators, although their status is not clearly delineated. We assume that the two members of the team with master's degrees are what are referred to in the report as research associates. The individual senior authors are, generally, well published and obviously experienced in cancer epidemiology but not in occupational cancer epidemiology, which is a rather specialized field. One of the investigators does have more than one publication directly related to occupational epidemiology (Dr. Marrett) but her predominant interests lie in ultraviolet exposure and skin cancer. Another (Dr. Krieger) is a distinguished social epidemiologist who also has a small discernable body of work related to occupational epidemiology. Another (Dr. Sullivan) had none but is interested in colorectal cancer. (We assume that Drs. Chaudry and Do, who have few publications between them, are graduate

students.) There is no evidence from the Medline search that members of the team, individually or collectively, had been engaged in a similar project before this assignment.

The report

This general lack of experience on the part of the team may explain some of the anomalies in this report, which are unusual and often appear naïve. The individual team members may have been at a disadvantage working in an unfamiliar field, perhaps being unable to evaluate the logic behind the previous reports and the contextual issues that are critical to interpreting this literature.

The Background section of the report is extremely terse, almost schematic. In discussing (very briefly) the limitations of occupational epidemiology, the introduction to the Background section fails to mention the problems of the healthy worker effect (mentioned in passing in the Discussion), misclassification bias (a more likely cause of underestimation), the proper exposure metric (a central problem in firefighters studies) and confounding exposures. There is no mention of the central problems in firefighter research: the issues of changing combustion products and of personal protective equipment.The introduction does not convey a grasp of the complexity or of knowledge of common problems and issues associated with assessing risk arising from occupational exposures.

The literature on firefighters is very large and uneven, generally requiring careful evaluation and integration. In this study report, however, there is no general literature review, only a superficial discussion of the toxicology of relevant exposures and no overview of other occupational hazards. Many of the word choices are peculiar and not idiomatic (e.g. "after the fire is exhausted") and the syntax is unusual ("assessing relationship between...").

There is a useful (but very brief and incomplete) subsection on "firefighter characteristics", by which the authors apparently mean lifestyle characteristics. There are other characteristics of this working population they do not mention, such as the low turnover, the frequent occurrence of sideline employment ("moonlighting"), the fitness requirement and the ethnic and demographic profile of the occupation. (This has not been well documented but it is our impression, gleaned from going through personnel records, that at least in Alberta, this occupation has been dominated by British immigrants – not Irish, as in many cities in the US –

and Canadian-born men of working-class backgrounds who are very stable in residence and tend to retire locally or to BC.)

On page 2, the authors state "studies have suggested an underestimation of occupational cancers because occupational hazards are not the subject of systematic study." Some occupational hazards certainly have been investigated systematically (e.g. asbestos) and lack of systematic investigation does not imply underestimation (it may imply selection bias that would overestimate the risk). This may be an error: the writer may have meant to say that not all occupational hazards are adequately studied and so total risk of cancer arising out of occupation is underestimated. However, if this is what the writer intended it is not an argument that is easily applied to firefighters because the literature is rich in relatively well-conducted studies for this occupation. It would be more accurate to say that the risk of occupational cancer in firefighters is underestimated because exposure assessment is imperfect, potential biases almost all lead to underestimation, and the risk estimates of many outcomes of interest are diluted by aggregation. It is unclear whether the team understands this.

The Background section also makes no mention of the standard of certainty applied to the evidence. The fundamental principle of workers' compensation, which is the balance of evidence, is nowhere mentioned. Apparently by default, the team applies a scientific standard of certainty (95%) to a problem requiring balance of probabilities (50% + 1). It is unclear whether they were aware of this fundamental assumption, as it is nowhere mentioned.

The section on Objectives was originally stated, in the penultimate draft of the report, as a single sentence that reads "To determine if, based on the published literature, there is evidence to support a relationship between the occupation of firefighting and risk of specific cancers among firefighters." In the final version of the report this has changed. The "goal" is now stated as "to synthesize and analyze the scientific/medical literature regarding the causal association between the occupation of firefighting and specific cancers", listed as brain, kidney, bladder, ureter, colon, testes, non-Hodgkin lymphoma, leukemia, lung cancer in non-smokers and multiple myeloma. For a report with such serious implications, this brevity is heroic but the two sets of objectives (the one labelled "goal" is still in a section headed "objectives") are not the same. The first implies a standard of evidentiary strength, which this study report has attempted. The second implies a broad mission to interpret and integrate material across disciplines, which

this report has not done. More disturbing, the reader is left to wonder how something as basic as the objectives of the study could change from one draft to another.

Neither objective, in fact, is correct for such an exercise. Because the standard applied in workers compensation is the weight of evidence, not its sufficiency, the investigators are evaluating the wrong aspect of the question. They are determining whether the current body of evidence is sufficient or lacking to draw a conclusion with certainty. This is not helpful, for several reasons. First, the workers' compensation system requires resolution of cases in a timely manner on the basis of the existing evidence, not a judgement on whether the existing evidence is sufficient – cases are not going to wait for the evidence to improve. Besides, over the last five decades the weight of evidence for disease outcomes associated with firefighting has generally grown stronger, not weaker. The passage of time, in other words, is demonstrating new likely associations as evidence accumulates. Second, the evidentiary base for occupational risks among firefighters is as complete as it is for any other common profession: it is therefore rather ingenuous to fault it for being incomplete. Third, the weight of evidence is not the standard used in this report, which therefore irremediably biases its findings against the claimant, in violation of the Workers' Compensation Act, which requires that the benefit of the doubt be given to the plaintiff.

The team may be inclined to respond that sufficiency of evidence is in fact the criterion used for acceptance of claims under certain programs. However, if they did, they would have to explain why such an approach would apply here when the adjudication criteria for workers' compensation are already very specific in requiring a balance of probabilities. They would also be obliged to explain that such programs, such as the US Department of Veterans' Affairs Vietnam Veterans Agent Orange compensation program and the US Department of Energy's compensation program for workers exposed to chemicals in the nuclear weapons industry during the Cold War, are grounded on a completely different principle. They do not require balance of probability, but evidence of substantial risk and they are intentionally biased in favour of the applicant for reasons of public policy and to alleviate the burden of illness after public service. Both programs require the totality of evidence to be taken into account, not just cohort mortality or cancer incidence studies, and freely admit toxicological evidence.

The section on Methods presents problems for the careful reader. In practice, the methodology is a simple statistical algorithm that is applied much like a cookie cutter to the

overall findings in a set of selected studies, ignoring relative strengths and features within the studies chosen and discarding the more detailed information found in the more extensive studies.

The penultimate draft stated that the Cancer Care Ontario study also intended to accept unpublished reports, which presumably have not been peer reviewed, and indicated an intention to treat them as equal to peer-reviewed publications. This has been dropped from the final draft, with no explanation or clarification.

The search was restricted to English language reports which, as a practical matter, is satisfactory because the one critical report that was originally published in another language (Tornling's report on firefighters in Stockholm, which originally appeared in Swedish) was later published in English.

The subsection on exclusion criteria labels three studies on firefighters in the Northwest US as "duplicate" but this is incorrect. The three represent attempts to estimate risk more accurately by different means and with different local firefighter groups and are therefore better characterized as overlapping; they are not duplicate studies in the usual sense.

The description of quality assessment is wholly unsatisfactory. The Quality Assessment procedure is not specified, only that a three-point scale was used "for each dimension", but what is meant by "dimension" is unclear. (In the prior section there are two lists of characteristics and parameters for which data were abstracted but no "dimensions" of technical quality.) The Methods description states that each article was reviewed by one "scientist" with expertise in the area of occupational and environmental epidemiology (which, as noted, is limited in this team) and one "research associate", who can be assumed to be inexperienced in the field (see above). Thus, for all practical purposes, each paper was reviewed by one person who may or may not have had more than superficial experience in occupational and environmental epidemiology.

The report lists a "number of issues raised" with respect to cohort studies but does not make it clear that most of the studies omitted are old and that Deschamps et al. [8] was only a preliminary study conducted to support a future cohort study.

The study team omitted all PMR studies indiscriminately, including Burnett et al.[5], which is a special case that overcomes, through sheer numbers, many of the limitations of more conventional PMR studies. (Burnett et al. is described more fully below.) Burnett et al. was also conducted in large part as a test of a hypothesis suggested by an earlier study (Guidotti, 1993) [9] and confirmed the result (elevated risk of cancer of the kidney) in a different and much larger

population. Thus, in omitting Burnett et al., the team threw out the closest thing to hypothesis testing in the firefighting literature, at least before the recent studies on testicular carcinoma. They may not have realized this at the time.

The team also fails to identify the considerable differences among the studies and the patterns that they show. For example, Beaumont et al. [10] is a consistent outlier among studies of firefighters, recognized as such by workers experienced in the field, but this is nowhere mentioned and appears not to have been noticed by the team. Because the team does not recognize or appreciate these differences, they appear not to have noticed an important characteristic of the better studies (including Hansen [11], L'Abbé/Aronson [12], Guidotti [9] and Baris [13]) which is that the more refined the exposure assessment, the higher the risk estimates for plausible subgroups at risk. This general tendency suggests that as exposure assessment is improved, risks are better defined and the estimates increase. This, in fact, is one of the tests epidemiologists apply to data to determine if there is significant confounding and to correct the effects of misclassification bias. This observation is explored in greater detail below for specific sites. The team does not appear to have applied this basic principle or to have noticed the trend. Given their general expertise in exposure-related disorders in other fields, however, they must understand these principles since the same principles apply in the sun-exposure and dietary studies in which they are more experienced.

Of greatest concern, however, is the basic methodology. A simple algorithm for meta-analysis was applied to the surviving studies in the database, without regard for the nuances of study design, exposure assessment or validity of the diagnostic rubric. The entire procedure is described on a page. There is no effort to understand the biology of the disease or the reasonableness of the outcomes that were "grouped into similar site groups using ICD codes." This appears to be a case of having only a hammer and all problems therefore looking like a nail.

The last subsection (3.6) in the Methods section features "Criteria for Conclusions". These are rather general guidelines, some of which resemble the Bradford-Hill criteria and some of which deal with issues of interpretation (such as, the "likelihood that study results are due to uncontrolled confounding or other methodological problems"). Although it is quite valid to provide room for interpretation, the authors are silent on how they came to these conclusions and who did the interpreting and by what consistent framework. It is also of great concern that these criteria were not inserted until the last draft: if they were truly operational criteria for

establishing conclusions of the study, they should have been established at the outset and not added later.

The Table of Criteria (Table 5, p. 11) outlines the algorithm for each conclusion on evidentiary strength. These criteria (with the sole exception of evidence for a dose-response relationship) are based on summary risk estimates for the entire working population studied. This is not satisfactory. Too much information is lost by not considering classifications of firefighters, qualified by job assignment or duration of exposure or intensity of exposure, that may provide additional evidence, corroboration or identification of subgroups at elevated risk.

The Criteria also emphasizes "substances" to which firefighters may be exposed. In assessing an association with firefighting, relevant risk factors are not necessarily toxic exposures. For example, colon cancer may have little to do with combustion-related exposures but may still be work related if they arise out of work. Since firefighters live in the fire hall for the duration of their shift and cook there, dietary factors and stress-related effects on the gastrointestinal tract (well-documented to relate to intestinal motility) may mediate such effects and may well be work-related. Thus, the definition of a plausible causal exposure is much too narrow.

The Findings are presented in stereotyped subsections using essentially identical terminology. The risk point estimates and standard errors derived from the meta-analyses are presented in a log scale, which is not standard and which visually minimizes the appearance of variation, making it appear that point estimates "above" (to the right of) unitary risk are closer than they would normally appear on a linear scale. Oddly, the standard error bars are of equal length on both sides of the point estimate, although the scale is logarithmic. Is this an error?

From page 31 on, without caption, informative heading or discussion, there are a series of tables (starting with Table 6) that appear to summarize the studies reviewed and that treat exposure-response relationships based on the duration of employment, when available. This is not accompanied by text, which is peculiar for such a report.

The tables omit one major study in which detailed exposure-response data are available for many outcomes (Guidotti, 1993[9]) for no obvious reason and without explanation. The information on exposure in Guidotti, 1993, is provided only for kidney cancer and lung cancer in the form of duration of employment, although a refined exposure index, which takes into account actual opportunity for exposure by job classification for each year, was published in the study

and used to classify firefighters by relative exposure. The team apparently either overlooked this aspect of the study or intentionally ignored it, although it is a refinement of considerable importance. Likewise, the study team ignores the considerable detailed exposure-response data beyond duration of employment available in Baris et al.[13] This is unacceptable. It is an elementary error, the equivalent in occupational epidemiology of measuring dietary intake by how long a person has eaten a food rather than estimating actual consumption.

As noted above, the study team confined itself to duration of employment in those studies they chose to examine. Estimating relative exposure by different methods is important not only to assess exposure-response more accurately but, by determining whether the association is strengthened by improvements in exposure measurement, is a critical check on confouding. The study team does not apply this elemental principle of interpretation in occupational epidemiology and gives no reason why they fail to do so. This refusal to use all the information available is another fundamental failure of this study.

The Discussion section is superficial, abbreviated and highly unsatisfactory. On page 49, the authors mention the importance of exposure opportunity, yet they fail to use this information when it is available. This is intellectually questionable and undermines the credibility of the entire report. The authors have selectively used data that is most comparable from each study and have rejected or ignored data that are often most informative.

The Discussion section does not draw conclusions on causation, which is generally the point of adjudicating claims in the first place. Rather it, evaluates the strength of the evidence. While this is clearly an important aspect of interpretation for purposes of adjudication, it is not the only or even the most important step. That is to weigh the extant evidence and to determine the weight or balance of evidence. The study report does not do this, confining itself entirely to the assessment of strength of summary evidence, only, from comparable studies, rejecting those studies and subanalyses that do not fit the predetermined analysis plan. Thus, the job is less than half done, from the standpoint of proper adjudication.

The discussion of the healthy worker effect (p. 50) is naïve and ignores the literature on firefighters. The authors do not seem to appreciate that there are two healthy worker effects, constituting recruitment and retention bias. Firefighters are subject to both but the retention bias is attenuated by a historical pattern of job assignments that tends to protect firefighters who are less fit. Both patterns are strongest for cardiovascular disease and dimish rapidly after initial hire

for cancer, so that the two healthy worker effects are not as great an interpretive problem for cancer incidence and standardized mortality at later ages as they are for other outcomes and for proportionate mortality. Empirically, studies of firefighters have not shown the expected magnitude of the overall (combined) healthy worker for mortality, but there is evidence (discussed in Guidotti, 1993[9]) of an effect in younger age groups. The authors mention none of this and the discussion is highly superficial.

The Discussion section does mention the survivor effect. This is one bright spot in an otherwise highly disappointing Discussion section, because it acknowledges the related issues of competing mortality and "exhaustion of susceptibles" (a concept more often recognized in infectious disease epidemiology), which have previously been disputed in claims before the WCB of BC.

The Discussion section also has significant omissions. Crucially, it fails to address the issue from the standpoint of adjudication. The penultimate draft criticized the sufficiency of the literature, which is even so among the most complete for any occupation. This has been toned down in the final draft and the authors have reoriented the Discussion section toward methodology. It makes no effort to synthesize the literature, to assess major problems, to determine generalizability of conclusions or to summarize the findings.

Findings for cancer at specific sites

Despite the manipulations of statistical presentation, the findings are remarkably inconclusive. Given that workers' compensation is rather explicit in its requirement that the claim be based on the weight of available evidence, not its sufficiency for scientific certainty, this inconclusiveness cannot be very helpful.

Bladder. Bladder cancer is the first outcome considered. The team concludes that insufficient evidence is available, despite noting a consistent (but not statistically significant) excess risk. (The two studies that do not show an increase show consistently lower risk estimates for mortality overall and for other outcomes than other comparable studies in the literature, suggesting that they are different in some systematic attribute.) Certainly the association does not achieve conventional standards of statistical significance but the weight of evidence clearly does

suggest an increased risk. Bladder cancer is therefore an example of the most fundamental problem of the study report, which is that the study team has defined a criterion for "limited evidence" that is inappropriate for the adjudication process.

Brain. Remarkably, the authors come to the conclusion that there is limited evidence (in the penultimate draft the conclusion was that the evidence was "sufficient") to conclude that there an increased risk of cancer of the brain among firefighters. This conclusion is reached on the basis of evidence that, on closer inspection, is no stronger than that for bladder (with almost identical pooled risk estimates around 1.4) simply because there are a larger number of studies. (Recall that adjudication under workers' compensation requires consideration of the weight of evidence, not its sufficiency for scientific certainty.)

Colorectal. The final study report concludes that there is limited evidence of an increased risk of colorectal cancer among firefighters. This conclusion appears to have been modified during the course of the study, raising questions about the application of the criteria for a conclusion. Insufficient evidence to determine whether an association exists was originally reported for colorectal cancer in the penultimate draft. Inconclusive evidence to determine whether an association exists was originally reported for colon cancer and rectal cancer individually and together. Later, the addendum revisited these same outcomes and concluded that there is indeed evidence to support an association. The findings of the addendum carried over into the final report.

Kidney. This section was added to the final report, suggesting that it was omitted from the original analysis. The team concludes that there is no evidence of an increased risk associated with firefighting, despite two relatively strong studies with quite large risk estimates and confirmatory evidence from Burnett et al.[5] (which they do not consider), which is also reflected in Ma et al.[20] and a strong suggestion in a subgroup of Baris et al.[13]. Given that kidney cancer is rare and that few studies have the power to detect a true increase in risk, this is a heroic conclusion.

Leukemia. The team concluded that there was insufficient evidence to determine if there is an association. The team is correct in observing that leukemia is a heterogeneous group of diseases. (This observation was added to the final version: it does not appear in the penultimate draft.) They do not, however, use this information to interpret their findings or to point out the

methodological implications. The implications of this omission are described in detail later in this report.

Lung cancer. Despite elevations in three mortality studies, the authors conclude on the basis of their meta-analysis that there is "no evidence" of an increased risk of lung cancer among firefighters. They come to this remarkable conclusion on the basis of summary statistics alone, without considering the exposure-response relationships or the known differences in population characteristics. The implications of this superficial examination are described later in this report.

Multiple myeloma. The team concluded that there was insufficient evidence to determine if there is an association with multiple myeloma. The report fails to acknowledge that the same heterogeneity as previously noted for leukemia is also a feature of myeloma (and, for that matter, brain). No reason is given for this highly selective discussion. The penultimate draft placed a heavy emphasis on the association with bezene exposure (more so than for leukemia, inappropriately) but this has been removed in the final draft.

Non-Hodgkin lymphoma. The team concluded that there was insufficient evidence to determine if there is an association with non-Hodkgin lymphoma. The discussion of non-Hodgkin lymphoma is very abbreviated for such an important and complicated group of outcomes. Oddly, the penultimate draft acknowledged that this group of disorders "represents a heterogeneous group of cancers of the lymphatic system, which may have different etiologies" but this observation, which is true, was omitted from the final report. The final report therefore treats the rubric as a single entity, which is inappropriate. This issue is discussed further later in this report.

Testicular cancer. The authors conclude that there is insufficient evidence to evaluate the risk of testicular cancer when all four studies show an elevated point estimate and three out of the four studies have demonstrated elevations over 1.5, one as high as 4.30. (Similarly, they make the same conclusion for bladder cancer when seven out of nine studies show elevations.)

The supplement

For completeness, this subsection will discuss the supplemental report that was submitted after the penultimate draft went to reviewers. It contains more detail on certain outcomes and issues than appears in the final study report. The supplemental report appears to have been rather unresponsive to the questions put to the team by the WCB.

Question 1 requested the scale used in the rating system. Neither the instrument nor the "scale" used in the rating system was apparently provided to the WCB initially. The description and the instrument provided as an appendix to the addendum are inadequate to reconstruct the work and therefore falls short of the normal scientific standard, which is that a description of methodology should be sufficient for replication. An extraordinary statement is made: "The ratings of these three aspects" ("quality design" – possibly quality of design is meant, measurement and analysis) "were used to facilitate discussion during the consensus process." One must ask: What consensus process? What methodology is there, exactly, for achieving "consensus"? Does consensus mean, as it usually does, unanimity in a final decision notwithstanding differences in interpretation or opinion, or is the word being used here, as implied in the text, as a synonym for majority?

Question two asked for the criteria for quality assessments. The authors do not offer the actual criteria. They provide only general descriptions suggesting subjective discomfort with the methods because of the perception of possible bias. An extraordinary statement is made that "Studies rated as 'weak' by both reviewers, or by consensus if there was disagreement, were eliminated from further analysis." The only possible reading of this statement is that some studies were evaluated by two only readers (presumably only one of whom was experienced, if in the Methods section is literally accurate). If so, in this case consensus does not mean unanimity but a majority (of whom? the experienced reviewers or everybody?). It also means that the evaluations were subjective.

Question 3 dealt with cancers of the brain and nervous system. The team gives an answer that is not responsive to the WCB with respect to exposure-response relationships and also contradicts itself. They say that good studies show such a relationship but that they chose not to recognize it because it is not consistent in all or most studies, possibly because the numbers are small and so the literature may never be able to show it. This is not helpful.

Question 4 pertains to lung cancer. Asked directly whether the risk of lung cancer is likely to be elevated among non-smoking firefighters, the team is again unhelpful, commenting on the sufficiency of the literature rather than the weight of evidence. (There are no studies of non-smoking firefighters, nor are there likely to be.) They do admit, however, that smoking rates are not obviously elevated among firefighters but fail to draw the obvious conclusion that this means that those studies that do show an excess risk are probably not confounded by smoking.

Question 5 pertains to the risk of cancer in full-time/part-time/volunteer/forest firefighters. The team states that they cannot respond because there are no relevant data separating these groups. They are mistaken. Eliopulos[14] is a high-quality study, included in their report, that specifically examines the risk in wildfire firefighters fighting brush fires in the sparsely populated state of Western Australia.

In the Addendum to Methods, the team provides a method of examining colon, rectal and colorectal cancers. (We allude to this above in the section on findings for each set of outcomes.) In the original report, there is an implied criticism of studies that do not separate the two sites. In this addendum, the team admits that there is a high probability of misclassification, so that a reported separation may in fact be misleading. Also, the differences in risk factors between colon and rectal cancers are primarily associated with lifestyle, not diet or genetic predisposition, which are shared risk factors. A large difference in rectal cancer sufficient to artifactually create an excess in colorectal would imply a substantial difference in distribution of pertinent lifestyle risk factors between firefighters as a group and the general population. There is no evidence for this.

Overall, even taking into account the additional information supplied by the Addendum, this report has surprising gaps and deficiencies for the work of an experienced team. It is noteworthy that this report appears much less comprehensive and less developed than the Industrial Disease Standards Panel Report of 1994[15], with which it frequently disagrees.

The Rationale of Adjudication

The logic of assessing causation in adjudication and civil litigation is not the same as for concluding causation in a scientific investigation or criminal prosecution. In adjudication and civil litigation, the burden on experts is to determine whether it is more likely than not that the evidence favours one side or the other. In worker's compensation, experts are required to provide evidence for or against the proposition that the claimant's injury arose out of work and to determine the weight of evidence. All hinges on the weight of evidence in the individual case (with the benefit of the doubt going to the claimant if the odds are even). In workers' compensation, the weight of the available evidence, which is usually incomplete, must support a decision that it is more likely than not that the claimant's condition arose out of work. [9]

In civil litigation and in almost all adjudication systems, experts are neither required nor expected to prove causation to a near certainty. They are, in effect, asked to practice epidemiology "as if" the standard of certainty were 50+%, rather than 95+%. This does not represent a distortion of scientific standards. Rather, it is a legal requirement within a system that vests decision-making authority in the court, the adjudicator or a jury, but not the expert.

Merely demonstrating that there is an elevated risk of a particular outcome among members of an occupational group is therefore not enough. It is also necessary to demonstrate that the individual circumstances of the claimant are consistent with the premise that the condition arose out of work. When the weight of evidence favours causation in an entire occupation, there is a basis for presumption.

Presumption is, simply, the doctrine that claims should normally be accepted when, all other things being equal, a claim received from a worker in a certain occupation is demonstrably more likely than not to have arisen out of work, whether or not it is possible to prove the association in the individual case. This occurs when the risk for the group is at least doubled compared to a relevant reference population.

Doubling is important. An SMR of 200 is equal to a risk attributable to conditions of work equal to of the risk for the general population and represents a high degree of association. It means that the attributable risk due to work is at least equal to the shared risk from other factors in life, including environmental factors associated with living as a member of the community. Applied to firefighters pursuing a claim in a workers' compensation system, an SMR of 200 implies that, all other things being equal, the risk of a firefighter developing a cancer (such as bladder) from work-related exposure is approximately equal to that of the risk of the same cancer in everyday life. Therefore, it is a statistical expression of the standard that it is "more likely than not" that the condition arose out of work. This constitutes the basis for a presumption, under which all such cases arising in workers in a particular occupation would normally be considered work-related unless there is evidence to the contrary or an alternative cause of greater certainty in the individual case.[6,15,16]

On the other hand, there is statistical error and bias that may obscure a true doubling. A risk that is elevated to a degree approaching a doubling, and that becomes more elevated as the exposure assessment improves (implying reduction of a confounding association) is likely to be,

in fact, a true doubling. As a practical matter, it is not possible to distinguish between 2.0 and 1.8 or 1.7 or, for that matter, 2.4 in most epidemiological studies.

A presumption assumes that, all other things being equal, most cases of a certain type among workers in a given occupation are associated with occupational exposure, even though it is not possible to determine which among the individual cases. Presumptions are normally rebuttable, meaning that the adjudicating body may also examine evidence in the individual case that supports or calls into question the individual claimant's risk and the relationship to work. For example, a strong family history of the disease, the presence of a strong personal risk factor (usually smoking) or a work history that is incompatible with latency would all be grounds for rebuttal.

Presumption is a means of achieving consistency, administrative efficiency and fairness in the management of claims. Claimants must generally demonstrate that they belong to the group and satisfy certain criteria such as duration of employment and latency. Rebuttal criteria must be addressed with evidence or convincing argument. In the end, it is still the merit of the individual case that matters but the presumption facilitates adjudication. Population attributable risks are useful as crude estimates of individual risk, serving as best estimates only where there is no specific information on which to estimate individual risk. Epidemiology contributes to the weight of evidence but the case is decided on its own merits.

From the standpoint of social policy, a policy of rebuttable presumptions accepts that nonmeritorious cases will be inevitably compensated in the interest of the greater good of ensuring that all meritorious cases are compensated. A policy that rejects all such claims or that applies arbitrary additional criteria, such as restricting compensation to non-smokers, will inevitably deny benefits to some, usually many, claimants whose disorders did in fact, arise from work but who cannot demonstrate the association. To accept all such claims will, predictably, include some cases, usually many, in which the disorder did not arise from occupation.

The Evidentiary Base

In this report, the risk estimates will be presented as they were reported in the original paper. SMRs are given to three places, without decimals, or expressed as relative risks as in

Baris et al.[13] Relative risks are given as decimals, with no qualification. Odds ratios are given as decimals and identified as such.

The literature up to 1994 has been extensively reviewed in two principal sources. In 1994, the Industrial Disease Standards Panel of Ontario[15] produced a widely-quoted report designed to identify candidate conditions that merit occupational disease presumptions in that provinces' system of workers' compensation.[14] We published a similar analysis in 1995, differing in detail but reaching similar conclusions, which are summarized below.[16]

- Lung cancer: There was evidence by 1995 for an association but not of sufficient magnitude for a general presumption of risk. We suggested that a presumption be considered for non-smoking firefighters.
- Cancers of the genitourinary tract, including kidney, ureter, and bladder: The evidence by 1995 was strong for both an association and for a general presumption of risk.
- Cancer of brain: Incomplete evidence by 1995 strongly suggested a possible association at a magnitude consistent with a general presumption of risk.
- Cancer of lymphatic and haematopoietic tissue: As a group, there was some evidence for both an association and a general presumption or risk. However, the aggregation is medically meaningless. We therefore recommended a case-by-case approach.
- Cancer of the colon and rectum: There was sufficient evidence to conclude that there is an association but not that there is a general presumption of risk.

The evidence supporting these recommendations is presented in these reports and will not, with the exception of leukaemia, be revisited here.

It is important to recognize that although most cohort mortality and incidence studies of firefighters are similar in their methodology, there are considerable differences among them in cases lost to follow-up, reference population, exposure assessment and analysis. For example, Beaumont, et al. (1991)[10] presents exceptionally low overall and consistently lower site-specific standardized mortality ratios for firefighters than other cohort studies of firefighters in the literature. If the overall mortality is normalized, the site-specific risks presented by Beaumont et al. appear more in line with other studies. Hansen et al.[11], on the other hand, used an unusual reference population (military recruits) and Demers and his various colleagues[17, 18, 19] tried several reference populations (including police) and various combinations of cohorts. The richness of the literature cannot be appreciated without understanding these differences. Without

a close examination of these study characteristics as well as basic design, the full value of the information contained within cannot be applied to problem of occupational risk in firefighters.

There are reasons that argue for emphasizing some studies over others for certain purposes. One study well much relied upon in the present report and in previous publications is Guidotti (1993)[9], which the author of this report carried out and therefore knows well. This study needs to be understood for its strengths as well as its shared, generic weakenesses (no information on smoking). Guidotti (1993) is essentially two replicate studies (examining two cities of equivalent population and numbers of firefighters) in one, providing the possibility of internal comparisons; was conducted in a population with documented exceptionally low smoking rates for most of the period covered by the study and relatively low mortality from lung disease; features an unusually high number of cases followed to "extinction" of the cohort (and thus reflects lifetime risk rather than risk up to retirement and relocation, or loss to follow-up); and presents two alternative exposure assessments, one factoring in opportunity for exposure based on job classification. These characteristics are typically considered advantages in epidemiological studies. That is why this study is emphasized, beyond personal attachment.

Since 1995, there have been several additional major studies that have contributed to the world literature on firefighters. They are summarized below without reference to the earlier work.

Burnett et al.[5] conducted a very large proportionate mortality study on firefighters in 27 American states from 1984 through 1990, using data from the National Occupational Mortality Surveillance system. Limitations of these data are partially overcome by the sheer size of the database, 5744 deaths among white male firefighters, which is far beyond what may be achieved in any one cohort study. This study is an example of population surveillance for occupational disease, which we have advocated elsewhere.[3] This study was originally conducted, in large part, as a test to confirm the findings of Guidotti et al. (1993) and did so.

Deschamp et al.[9] studied the recent experience of relatively small number of fire fighters in Paris from 1977, as a prelude to a longer-term cohort study. An elevated SMR was found for respiratory cancers (1.12), gastrointestinal cancers (1.14) and genitourinary cancers (3.29) among other findings. However, the study is anomalous in several ways, uniquely demonstrating an elevated mortality from stroke (1.19) and a very low overall mortality (0.52), the lowest reported to date among firefighters. Further experience with this cohort is required to interpret the findings.

Ma et al.[20] conducted a large study using the same database as Burnett et al.[5] to explore race-specific disparities in cancer mortality. For this study, the NOMS database was extended by three years to 1993 but lost data from three states that were removed. Race as coded on the death certificates yielded 1817 deaths of white firefighters and 66 deaths of black firefighters. As expected, the overall results were similar. Of greater interest is the pattern of race-specific elevations. If an environmental or occupational factor is the major risk factor for a certain type of cancer, one would expect elevations in both white and black firefighters.

Bates et al.[21] reported a study on firefighters in New Zealand from 1977 to 1996, conducted to investigate the observation of a cluster of testicular cancer. This elevation was confirmed independent of the cluster. This study is unusual in reporting both cancer incidence and mortality. It also reports one of the lowest mortality ratios reported for firefighters (0.58), suggesting a uniquely strong healthy worker effect. The healthy worker effect is much stronger for cardiovascular disease than for cancer but a mortality level this low suggests that underlying risk factors such as smoking may be hugely different. The authors caution that matching to mortality data and cancer registration data may be incomplete prior to 1990 and suggest that they have greater confidence for findings after this date. Bates et al.[11] observed no significant elevations except for testicular cancer. They found a marked increase in testicular cancer and nonsignificant elevations in incidence in the 1977 – 1996 cohort of cancers of interest: lung (1.14, 95% 0.7 – 1.8), which showed a modest increase with duration of service, bladder (1.14, 95% CI 0.4 – 2.7), brain (1.27, 95% CI 0.4 – 3.0), and "myeloleukemia" (1.81, 95% 0.5 – 4.6), but not kidney (0.57, 95% CI 0.1 – 2.1). Limiting the analysis to the 1990 – 1996 subcohort, however, they found the increase in testicular cancer but a deficit in most of these same cancers, except for brain (1.59, 95% CI 0.3 – 4.6), and no kidney or "myeloleukemia" cases. A strikingly different picture is observed in the pattern of deaths, however. Mortality among firefighters in the 1977 – 1996 cohort is elevated for bladder cancer (2.73, 95% CI 0.3 – 9.8) but less than expected for lung (0.86, 95% CI 0.4 – 1.6), brain (0.68, 95% CI 0.1 – 2.4) and "hematopoietic cancer" (0.72, 95% CI 0.2 – 1.8), and these use no deaths from testicular cancer. The discrepancy between incidence and morality in cancers with a high case mortality, such as lung, is an anomaly. However, all numbers are small and the authors are candid in describing limitations of the database.

Baris et al.[13] conducted an exemplary cohort mortality study. This study should be accorded great weight because it has exceptional power, spans most of the 20th century, and has the most complete follow-up. The study therefore merits description in detail.

The cohort consisted of 7789 Philadelphia firefighters employed from 1925 to 1986 compared to US white male rates, comprising 204,821 person years of follow-up. The men were hired in their late 20s (on average) and worked on average for approximately 18 years, with an average of 26 years follow up. Baris et al.[12] examined their cohort by age, duration of employment, job assignment and by number of runs to fight fires (enumeration of responses from the firehall) in three broad ordinal categories. There were 2220 deaths among the members of the cohort.

All causes of death and all cancers were approximately equal to the expected rates for all U.S. white males. The authors did observe statistically significant excesses for colon cancer (SMR 1.51; 95% CI =1.18-1.93). Nonsignificant excesses were reported for cancers of the buccal cavity and pharynx (1.36; 95% CI=0.97, 2.14); for non-Hodgkin lymphoma (1.41; 95% CI=0.91,2.19); for multiple myeloma (1.68; 95% CI=0.90-3.11) and for lung cancer (1.13; 95% CI 0.97-1.32). With >20 years of firefighting, the following cancer sites showed elevated risks: colon cancer (1.68; 95% CI 1.17-240); kidney cancer (2.20; 95% CI 1.18-4.08); non-Hodgkin lymphoma (1.72; 95% CI 0.90-3.31); multiple myeloma (2.31; 95% CI 1.04-5.16); and benign neoplasms (2.54; 95% CI 1.06-6.11).

Baris et al.[13] also developed a direct index of exposure by assessing risk by volume of firefighting runs over the career of firefighters. Cancer of the pancreas showed a possible exposure-response relationship which rose from 1.02 for low to 1.17 for medium to 1.61 for high exposure. Although there were no other tumour sites with an exposure-response gradient, comparing low exposure (1.00) to high exposure reveals that, several other cancer sites demonstrated increasing risk: stomach, 1.20; pancreas, 1.42; leukemia, 1.22; and benign neoplasms, 2.06. The authors also evaluated career exposure to diesel fumes, including unexposed. Although there were no continuous exposure-response gradients, several sites demonstrated increasing risks in the medium and high categories compared to unexposed: buccal cavity and pharynx, prostate, brain, multiple myeloma, and leukemia.

Genitourinary Cancers: The "normal" case

Genitourinary cancers represent the conventional situation, in which individual diseases are more or less satisfactorily classified and risk estimates probably do reflect the experience of the group for the individual cancers. Perhaps for this reason there seems to have been more widespread acceptance of claims by firefighters in this class than for other outcomes. The data are reasonably easy to interpret by tumour site.

Bladder cancer

Burnett et al.[5] found no elevation for bladder cancer. The PMR was 101 for firefighters dying under the age of 65 and 99 for those dying at or over the age of 65. With 9 and 37 deaths, respectively, this is a large collection of deaths by bladder cancer. Using the same database, Ma et al.[20] reported that a not-quite statistically significant elevation of 1.2 was observed for bladder cancer among white firefighters and an elevation (but based on a single case) for black firefighters.

For bladder cancers, latencies tend to be shorter and more variable than for other solid tumours. Aniline dye workers in the 1940's and 1950's showed a latency as short as seven years, presumably due to high, constant exposure which may have compressed the latency period to its absolute minimum. This is not plausible for firefighters. The exposure of firefighters to potential bladder carcinogens is much less than for chemical workers in the 1920's. In our data from Alberta[13] bladder cancer did not appear before age 60 or before 20 years of service and showed a very long peak latency of 40 years. Baris et al.[13] reported a slightly elevated SMR of 1.25 for bladder cancer, with greatest risk being among those hired before 1935 (SMR=1.71 95% CI=0.94,3.08), and among those with greater number of runs during their first 5 years employed (SMR=2.59, 95% CI=0.64,9.84). It would be difficult to accept a latency under 10 years for bladder cancer in a firefighter but the literature from other occupations does not rule out latencies under twenty years. One might expect that the duration of service associated with risk among firefighters to be on the order of 15 years.

Kidney cancer

Burnett et al.[5] found a marked elevation for cancer of the kidney. The PMR was 141 for firefighters dying under the age of 65 and 144 for those dying at or over the age of 65. With 24 and 53 deaths, respectively, this is a large collection of deaths by kidney cancer. Using the same database, Ma et al.[20] reported a borderline statistically significant elevation of 1.3 for cancer of the kidney among white firefighters. No cases were observed for black firefighters.

The standard cancer epidemiology text Schottenfeld and Fraumeni[22] cites several studies in which a near doubling of risk is associated with duration of employment less than ten years, among the aluminum workers exposed to polycyclic aromatic hydrocarbons. These are likely to be the responsible carcinogens in firefighting. In data from Alberta[9] a marked elevation in risk for kidney cancer was visible in the category 10 – 19 years of employment. Baris and co-workers[13] reported a doubling of risk with an SMR=2.20, 95% CI=1.18, 4.08 among those employed for 20 or more years.

It is not clear that kidney cancer follows the same pattern as bladder cancer and latency has not been as intensively studied for kidney cancer. On the basis of current understanding and the literature on firefighters, it might be difficult to accept a latency under 15 years, just on the basis of the time required for a solid tumour to proliferate, but latency periods less than 20 but greater than 15 would not be unreasonable.

Testicular Cancer

Bates et al.[21] found a standardized incidence ratio of 3.0 (1.3 – 5.90) for testicular cancer among firefighters in the New Zealand city of Wellington. Stang et al.[23] reported similar findings from northern Germany, although their odds ratio of 4.3 (0.7 – 30.5) was not statistically significant. Such high risks are unlikely to be confounded by differences in the prevalence of cryptorchism (the major known risk factor), smoking (not known to be associated with testicular carcinoma) or other plausible alternative risk factors. In their community-based study of testicular carcinoma, only four firefighters and three controls were firefighters out of 269 and 797, respectively, making the power of their study very limited. Stang et al.[23] also reported on duration of employment. Of the four cases, two had been employed as firefighters more than 20 years and two for less than 4.

There are five basic tissue types of testicular cancer, the most common by far being seminoma (about 95%). Bates et al.[21] does not specify the histology of the tumours.

Stang et al.[23] reports that of the four in their study, two were embryomas, an unusually high frequency, which suggests, but does not prove, that this type (which is also found in mixed germ cell types) may be uniquely associated with occupational risk. The evidence is too weak to rely on, however, without replication.

Biological credibility for the association, however, comes from the observation by Olshan et al.[22] that the offspring of male firefighters (the vast majority are male) are at significant and substantial elevated risk for birth defects, specifically common cardiac anomalies (for atrial septal defects, an odds ratio of almost 6). Such a finding, implying a congenital birth defect mediated by a male factor, points to an effect at the testes or, less plausibly, in seminal fluid.

Given the totality of the evidence, it is reasonable to establish a presumption for testicular carcinoma on the basis of current evidence. However, given the methodological limitations of Bates et al.[21] and the lack of available evidence on exposure, tissue type of the tumours and latency, no further guidance can be recommended. Testicular cancer was not considered in earlier studies and an excess may have been hidden in aggregate figures for genitourinary cancers.

Testicular cancer represents a good example of the "first case" problem. When the first case of a previously unrecognized association is asserted in a legal action or a claim is filed, the literature is undeveloped and therefore does not support it. The first case is almost always denied. If the case is decided in litigation, this closes off access to any future remedy because the case has already been decided. Unless there is a provision in a workers' compensation system that requires the system to reopen claims, the rejected claimant goes without compensation regardless of the subsequent accumulation of evidence. A publicized first case often stimulates further research but this usually comes too late.

Brain: Many diseases in which one group predominates

Cancers of the brain arising from brain tissue are relatively rare and may include twenty or more individual types. Each type may or may not be a different disease, with its own risk factors. Epidemiological studies do not distinguish among them because they are individually rare, subject to miscoding and are aggregated into a more general ICD code when they are

reported. The most common type of "brain" cancer is glioma but this type only constitutes about half of the total. Meningiomas, which are not usually malignant, do not arise from brain tissue and are not obviously associated with environmental or occupational exposures, are often counted as brain cancer. Gliomas (astrocytomas) are more likely to be associated with environmental and occupational exposures. The risk of brain cancer as an aggregated category is increased in many studies but this risk is probably diluted by inclusion of cancers (and meningioma) that are not associated with environmental or occupational factors.[22] This leads to an inherent bias to underestimate the risk for that subset of cancers that may have a true association with firefighting. Analysis by specific tumour type might identify which, if any, is associated with the risk but these cancers are uncommon and such a study would be very difficult; require large populations and will not be done anytime soon if ever. A different approach is required, inferring risk for the predominant type from the combined risk for the group. Ma et al.[12] reported that no elevation was observed for brain cancer among white firefighters but a very large elevation, with a mortality odds ratio (MOR) of 6.9 (95% CI 3.0 – 16.0) was observed for black firefighters. Burnett[5] did not observe an elevation for cancer of the brain.

Baris[13] observed a relative deficit of brain cancer, with an SMR of 0.61 (95% CI 0.31-1.22). Risk did not appear to be concentrated in any subset of firefighters by assignment, number of runs or duration, although the highest SMR (1.18) was observed among firefighters with more than 729 runs in the first five years of duty. Because brain is an uncommon tumour site, statistical power is usually limited, even in large cohort studies. This study therefore does not contradict the findings of other studies that suggest an elevation in risk (upper 95% CI was 1.22), but it does not support them either. The weight of evidence to date, predominantly from earlier studies, suggests that the elevation in risk for brain cancer reflects a true risk which may be concentrated in certain subgroups, as demonstrated among black firefighters.

Demers et al.[17] documented a doubling or risk (SMR 257) at less than ten years of employment peaking at over a tripling (353) up to 19 years. Heyer et al.[18] also showed a near-doubling of risk (184) at less than 15 years duration of exposure. It is not clear what the minimum latency for a brain cancer might be, especially for rapidly-growing astrocytoma. It would be reasonable to assume that for aggressive brain cancers, exposure periods plus latencies may be under ten years in some cases.

Leukemia, Lymphoma, Myeloma: Many individual diseases in which no one disease predominates

This disease aggregation represents the most difficult case and remains refractory to efforts to tease out which individual diseases that are driving the elevated risk.

"Leukemia, Lymphoma, Myeloma" is a common aggregation in epidemiological studies. However, it is not a medically defensible aggregation of disease outcomes. The disease categories are distinct, although there is some overlap, and each category consists of individual disease with very different characteristics. Most epidemiological studies aggregate deaths or incident cases in these three broad categories, and even more commonly together, in order to achieve sufficient numbers for statistical analysis. However, the legitimate purpose for doing so must be to make a provisional assessment, to determine if there is an anomaly. When these aggregations are taken at face value, as if they were a single disease outcome, elevations in one disease or a deficit in another can easily distort the aggregate risk estimate.

Non-Hodgkin Lymphomas

Lymphomas are uncommon. They tend to contribute a small number of deaths in most studies and are difficult for epidemiologists to analyze. Because they are individually rare and many tend to manifest themselves at older ages, their relationships to environmental factors are more difficult to determine.

Epidemiological studies generally do not separate the various types, or if they do, divide lymphomas into simply Hodgkin's disease and non-Hodgkin lymphomas. Hodgkin's disease is actually a class of apparently closely related lymphomas that tend to peak in young adulthood and again at older age and have not been associated with occupational or environmental exposures or occupational risks. Non-Hodgkin lymphomas are a larger, more heterogeneous category and have long been known to be associated with many environmental exposures and occupations.[22, 24] Non-Hodgkin lymphoma is further divided, especially in older epidemiological studies, into the obsolete categories "lymphosarcomas" and "reticulum cell sarcomas".

This crude system obscures the level of risk that may exist for certain critical types of lymphoma. There are over 30 types of lymphoma recognized in the current classification system (the WHO and R.E.A.L. system). New types will be identified as immunological and genomic methods become more sophisticated. Different types of lymphoma are known to be associated with different occupational risk factors, including follicular cell lymphoma with the meatpacking industry and small cell lymphoma with solvent exposure.[25] Chronic lymphocytic leukemia, which is more accurately considered a lymphoma appearing in blood, was recently identified as a risk of Vietnam veterans exposed to herbicides on this basis, although leukemias in general, are not so recognized.[26]

If, as seems plausible, different environmental exposures are associated with different cell types of non-Hodgkin lymphoma, a truly elevated risk that arises, for example, from exposure to some constituent of combustion products, may be diluted by inclusion with all the other types of lymphoma, that have no association with the exposure. Analysis by specific tumour type might identify which, if any, is associated with the risk but these cancers are uncommon and such a study is probably not feasible for a single occupation.

Lymphatic cancers were separately addressed in Burnett et al.[5], which revealed an elevation for non-Hodgkin lymphoma. The PMR was 161 for firefighters dying under the age of 65 and 130 for those dying at or over the age of 65. With 35 and 66 deaths, respectively, this is a large collection of deaths by lymphoma. These cancers were also separately identified by Ma et al.[20] who found a statistically significant elevation of lymphatic cancer was observed among white firefighters, with a MOR of 1.4. Ma found no elevation was observed among black firefighters, based on a single case.

Baris et al.[12] observed a not-quite significant overall elevation for non-Hodgkin lymphoma, with an SMR of 1.41. While not achieving statistical significance, this rose to 1.72 for firefighters with 20 years or more experience and 2.65 for those assigned to ladder companies. The subset hired between 1935 and 1944 did show a statistically significant elevation of SMR 2.19 (95% CI 1.18-4.07). A reverse dose-response relationship was observed by number of runs, with the group experiencing the lowest number showing a significant elevation, with an SMR of 2.36 (95% CI 1.31-4.26), but no relationship was found with runs during the first five years. Baris et al.[13] found that among those employed more than 20 years, the SMR was 2.20,

95% CI=0.90,3.31). This suggests the possibility that these are true elevations in these subgroups.

Leukemias

Haematopoietic cancers (which affect the blood-forming organs, most particularly bone marrow) are generally known as leukemias. There are about a dozen well-recognized forms of leukemia, of which five or six predominate. Different environmental exposures may be associated with different cell types. Acute myeologenous leukemia is known to be associated with benzene exposure. AML is the most common leukemia in adults and this leukemia has been the subject of many studies. Individually, leukemias are relatively uncommon. A truly elevated risk of AML, which may arise from exposure to benzene in combustion gases, may well be diluted by inclusion with all the other types of leukemia, many of which may have no environmental association. Unless studies are conducted on specific leukemias among firefighters, this problem cannot be resolved and the risk within the class must be inferred from the available data.

Haematopoietic cancers were separately addressed in Burnett et al.[5], who reported a PMR of 171 for firefighters dying under the age of 65 and 119 for those dying at or over the age of 65. With 33 and 61 deaths, respectively, this is a large collection of deaths by leukemia. Ma et al.[10] observed no apparent elevation for haematopoietic cancers, with an MOR of 1.1. There were no cases among black firefighters. This is unusual but probably reflects the smaller numbers of black firefighters in the American population.

Baris found no overall elevation for the leukemias (SMR 83, 95% CI 0.50-1.37), not specified as acute or chronic or by type. A statistically significant elevation in SMR of 275 (95% CI 1.03-7.33) was observed for firefighters assigned to ladder companies only, but not to those assigned to both ladder and engine companies. A non-significant elevation was observed for those with a high level of runs in the first five years, with an SMR of 2.44 (95% CI 0.70-8.54) and with medium (but not high) levels of runs over a lifetime, with SMR of 2.50 (95% CI 0.56-11.10). These data are not compelling evidence for a true association in this population but do not rule it out. Because of power considerations, the study by Baris et al.[12] does not really clarify this issue.

There is also an important anomaly in the older literature. L'Abbé/Aronson and Tomlinson,[12] in a study of firefighters in Toronto, uniquely reported risk for types of leukemia. They observed an excess of "lymphatic" [lymphocytic] leukemia at 190 (42 – 485). This finding was highly influential in the IDSP report, but is anomalous. Acute myelogenous leukemia (AML) would be expected to be elevated in circumstances in which benzene is a hazard, not lymphocytic. These findings suggests that it is premature to limit the presumption to AML.

Although Ontario now recognizes lymphocyctic leukemia, the evidence presented by L'Abbé and Tomlinson[12] cannot be used to rule out the possibility of an association with AML. The evidence suggests (again, at the level of "more likely than not") that it cannot, be convincingly argued that only one form of acute leukemia, either myelogenous or lymphocytic, should be recognized. Lymphocytic leukemia is suggested by the empirical data, AML by the known toxicological profile of exposures experienced by firefighters. Thus, it is not possible to recommend a selective criterion that only recognizes AML, lymphocytic or, for that matter, only acute and not chronic leukemias.

Leukemias tend to have short latencies, on the order of five years or so. Short latencies and therefore duration of employment for leukemia are reasonable, on the order of four years to ensure that no errors of exclusion are likely.

Myeloma

Myelomas are B-cell lymphomas and malignant plasma cell dyscrasias. Baris et al.[13] found that increased with duration of employment, with 20+ years having a statistically significant SMR of 2.31, and a statistically significant SMR of 2.54 for engine company employment only, with some suggestion of correlation with medium and high diesel exposures (latter based on small numbers of deaths).

Interpretation

The weight of evidence for lymphatic cancer of the non-Hodgkin type and haematopoietic cancer suggests that the elevation in risk reflects a true risk in certain subgroups but these subgroups cannot be readily identified by usable criteria in adjudication. Thus, the earlier recommendations from IDSP[15] for a presumption, and by Guidotti,[16] for an implied presumption but with individual evaluation of each case, are not contradicted by the new

evidence. Because the individual disease risks cannot be separated, they must be taken as a group until more information is available.

Lung Cancer

Lung cancer presents a different problem. In this case, the risk associated with occupation is overwhelmed by the effect of cigarette smoking. A different approach must be used.

Lung Cancer

Lung cancer has been among the most difficult cancer sites to evaluate. Despite the obvious exposure to carcinogens inhaled in smoke[2], it has been difficult to document an excess in mortality from lung cancer of a magnitude and consistency compatible with occupational exposure. Respiratory protection has reduced individual exposure levels to combustion products since the 1970's, and this may be the reason that studies rich in recent person-years of observation, such as Baris et al[13] , do not observe elevations. Studies conducted in Alberta on fire fighters entering the fire service from 1927 to 1987 do show evidence for an increase in risk .[9]

Without question, cigarette smoking complicates the analysis, but the prevalence of smoking among fire fighters does not appear to be excessive compared to other "blue collar" occupations. A comparison that takes into account the prevalence of cigarette smoking is illuminating.

What is the Unconfounded Risk Attributable to Fire fighting?

Many studies have shown an excess of lung cancer on the order of 20 to 80% (i.e. SMRs around 120 or 180), a magnitude not uncommon in studies of other blue collar occupations with less plausible exposure levels.[27] However, the empirical findings on lung cancer from recent, well-designed epidemiological studies have been inconsistent.[16] One study from Denmark reported a standardized mortality ratio of 317 for older fire fighters but the comparison population was unusual and difficult to interpret[11]. Studies on cohorts from San Francisco [10] and Buffalo[28] showed no excess and even suggest a deficit. This might be expected if firefighters, on average, smoke less than the general population and there is some evidence for this.[29]

In 1995, we proposed that the true risk for lung cancer associated with fire fighting was probably on the order of 150.[16] This figure has been disputed. We suggested then that the true risk

has been underestimated in career fire fighters and both diluted and confounded by the effect of cigarette smoking, which is a much greater risk factor.

Virtually all extant studies that are positive, relevant, close to the primary data, large and well done seem to cluster in a band from an excess of 30% to 68%.[16] The principal exceptions are Baris et al. [13] and Vena and Fiedler [29]. Baris et al., despite a low overall risk (1.13, 95% 0.97 – 1.32) does report suggestive elevations in certain subgroups, notably fire fighters with less than 9 years of service (1.52, 95% CI 1.16 – 2.01), those assigned to engine companies (1.18, 95% CI 0.93 – 1.51), and those hired before 1935 (1.30, 95% CI 0.97 – 1.73). Vena and Fiedler [28] present one of the lower overall risks in the fire fighting literature (0.94, 95% CI 0.62 – 1.36) but their data show a possible exposure-response relationship with duration of employment (a near-monotonic increase of 0.14 relative risk for each of five decade of fire service, nonparametric $p < 0.07$) and a statistically significant excess (at $p < 0.01$) for fire fighters with more than 40 years of fire service (1.29). Heyer et al. [18] reported an overall risk of only 97 (95% CI 65-139) but observed an elevated risk among fire fighters aged 65 years or more, when the incidence of lung cancer tends to peak. Thus, even in so-called "negative" studies there are hints of a possible association.

Among those studies that appear to be unequivocally "negative", Beaumont et al.[10] reports the lowest risk (0.84, 95% CI 0.64 – 1.08). This same study is unusual among the major studies because it also shows the largest healthy worker effect, the lowest overall mortality from all causes 0.90 and the lowest mortality rate cancer (0.95) an atypical age distribution and a high rate of cirrhosis.

At the other extreme is one study by Hansen et al.[11] in which an overall risk of 163 (95% CI 75 – 310) was accompanied by a tripling of risk (317) for firefighters aged 60 to 74. This is imaginative Danish study aggregated other occupational groups into a synthetic reference group. The artificiality of this construct makes the study difficult to interpret, however.

In our study of urban fire fighters in Alberta,[13] we found trends that we believe suggest a true SMR on the order of 150 in that population. Individually, these trends are not definitive but together they are highly suggestive. The overall SMR for lung cancer was 142 (95% confidence interval 91, 211), statistically not significant, and statistically indistinguishable from 150. However, lung cancer was elevated to an SMR of 167 among fire fighters entering the fire service in the 1960's, the most recent cohort at the time of the study for which the expected latency period had elapsed. This is not strong evidence, because it is based on only two cases, but the following cohort

of firefighters entering in the 1970's showed an even greater risk, 261 (although based on a single case). The risk of lung cancer also showed an exposure-response relationship in our data, with groups of fire fighters who had higher exposure opportunities and duration showing elevations on the order of 200. By duration of employment, an initially high risk for those with less exposure declined with duration of employment but achieved a doubling for those working 40 or more years (although only two firefighters were in that group). More persuasively, when duration of employment was corrected for exposure opportunity in job classification, the exposure-response relationship changed to suggest, following an initially high risk among probationary fire fighters or those unfit for duty, a more or less consistent but low elevation for the middling exposed varying around 150 (range 32 to 258), and a significantly elevated risk (408, $p < 0.05$) for those with more than 35 exposure opportunity-weighted years of employment.[13] Baris et al.[13] although negative overall, appears to show the same effect in the first 9 years. Unfortunately, the data from other studies cannot be disaggregated on the same basis as the Alberta cohort.

An important factor in the Alberta study, which was not appreciated at the time of initial publication, is that cigarette smoking is historically less of a confounding factor in Alberta than it has been in other populations. Subsequent studies of smoking-related lung disease outcomes suggest that smoking rates have been historically low in the province compared to the rest of the country and this is reflected in lower mortality from chronic obstructive pulmonary disease. In recent years mortality rates for smoking-related disorders appear to have converged with the rest of Canada as smoking rates in the rest of the country have gone down and those in Alberta have changed less dramatically. Again, this suggests, but does not prove, that the Alberta experience is less confounded by cigarette smoking than elsewhere.[30]

An anomaly of the Alberta data is that the excess was seen in one city (Edmonton) and not another (Calgary). In Edmonton alone, the risk was 201, the highest overall risk for lung cancer reported.[13] This represents an internal replication because the same study team collected data from both cities, matched against death certificates concurrently and analyzed both datasets simultaneously.

Taken together, and supported by the methodologically stronger studies in the literature, 150 seems to be a reasonable estimate of the true (unconfounded) risk for lung cancer among firefighters. The attributable risk fraction would therefore be on the order of 50% for firefighting as an occupation. For the average firefighter, therefore, the most likely estimate of the risk associated

with working as a firefighter would be about half that of the risk associated with living in the community.

The Non-Smoking Fire fighter

The findings of epidemiological studies are not necessarily applicable to the circumstances of an individual case. Claims under workers' compensation and other adjudication systems are generally required to be based on individual circumstances, not on broad generalizations, unless there is a relevant presumption and no unusual circumstances to rebut it. One of the individual factors of greatest practical importance is smoking.[6]

When lung cancer occurs in a firefighter who does not smoke, the relevant comparison is to the risk of other nonsmokers, not the population as a whole, which includes many smokers. For a non-smoking firefighter, the a priori risk for lung cancer is low. Is the additional risk attributable to fire fighting sufficient to achieve a doubling, the threshold for presumption? There is evidence that it is but some reasonable assumptions are required.

There is no study available that describes the experience of non-smoking firefighters. This is not unusual: it is difficult to identify or to partition out the risk of non-smokers in most epidemiological studies of occupational risk factors. Although lung cancer is rare in people who do not smoke, when it occurs it is usually adenocarcinoma. However, adenocarcinoma is also increased among smokers, so tissue type does not help as an indicator in the individual case.

In calculating the SMR or relative risk, both the numerator and the denominator typically include smokers. Smokers among the firefighters contribute the great majority of cases of lung cancer, as they do in the general population. Although their risk may be increased compared to similar smokers who do not fight fires, the increase is probably small in absolute terms, given their already increased risk from smoking, which is in the range of 5 to 10 times that of nonsmokers.[6,22] In the 1980's, perhaps 30 to 40% of firefighters smoked; the data available are sketchy but seem to be more or less in line with the general population.[29] The question therefore is how to estimate the relative risk of nonsmoking firefighters when most of the cases are already coming from smokers.

One may assume that, within a reasonable range of exposure, the magnitude of an increase in risk for lung cancer that is associated with a given exposure to combustion products from fighting fires would be the same for smoking and non-smoking fire fighters. This exposure

is added to the greatly increased risk sustained by smoking firefighters who receive much more intense exposure to similar and probably more potent carcinogens in cigarette smoke. [2,6] We may therefore assume a model in which the risk of exposure to combustion products from fires and the risk from smoking are roughly additive. For smoking firefighters, the risk arising from work is added onto the existing risk derived from cigarette smoking, which is about ten times the risk of lung cancer experienced by nonsmokers, overall. Thus, if the risk of lung cancer is increased by 50% for smoking firefighters, the proportionate increase in risk for non-smokers would be much greater, by as much as tenfold, because the same attributable risk is added to a much smaller baseline risk. Seen another way, the relative risk will be hugely increased if nonsmoking firefighters are compared to nonsmokers in the general population, because the risk attributable to occupation would be compared to a much smaller baseline risk for the reference population.

One approach to quantifying the risk of nonsmoking firefighters is to estimate that 40% (f = 0.4) of fire fighters smoke and that 60% do not (1 – f), that the relative risk of lung cancer for smokers is 10 times that of nonsmokers (R = 10.0), and that the relative risk (r) of lung cancer for fire fighters overall is 1.5. If x represents the attributable risk fraction,

$0.4(10+x) + 0.6(1+x)/0.4(10) + 0.6(1.0) = 1.5$. Solving for x yields an attributable risk fraction of 2.3. This translates to a relative risk for nonsmoking fire fighters of 3.3, comfortably above a doubling. The exact value is unimportant because of the compounded uncertainties; that it exceeds a doubling is what matters.

Another way to approach the problem is to determine, based on the same assumptions, what the minimum relative risk for the firefighters as a whole would have to be to reflect a true doubling of risk for nonsmoking firefighters. The calculations are similar and yield r = 1.22, which is comfortably supported by the world literature (whether or not the true risk is 1.5, as has been argued above). How sensitive is this model to underlying assumptions? Reducing the estimate of the proportion of the firefighting population that smokes to 30% barely changes the overall relative risk required to support the presumption, to 1.27. Reducing the estimate of the relative risk associated with smoking from 10 to 5, which is a low estimate and which intentionally biases the model against nonsmokers, increases the overall relative risk required to support the presumption to 1.38, still in line with the world literature and below the 1.5 level that probably represents the "true" risk. Again, the exact number is unimportant; what matters is that

the overall risks that would be associated with a doubling in the subgroup of nonsmoking fire-fighters falls into an area entirely consistent with the literature and therefore best evidence.

However, the most relevant comparison of all is a simple ratio to the nonsmoking population using the attributable risk function defined above. If a nonsmoking firefighter were compared to a similar population of people who also do not smoke, the expression would be $0.6(1 + x)/0.6(1.0) = 1 + x = 3.3$, which is the relative risk given above. (This is not coincidence, just the result of a mathematical identity. The group risk of people who do not smoke is defined as unity.) In other words, compared to nonsmokers as a group, smoking firefighters have much more than a doubling of risk. Again, the exact value is unimportant because of the compounded uncertainties; that it clearly exceeds a doubling is what matters most. Thus, it seems apparent that the available evidence supports the conclusion that the risk for lung cancer among nonsmoking firefighters is at least doubled compared to the general nonsmoking population.

Other Tumour Sites

There may now be sufficient evidence to consider colon cancer for a presumption.

Overall, Baris and co-workers found an SMR of 1.51 (95% CI 1.18,1.93), based on 64 deaths; there was no consistent dose-response for duration of employment nor for cumulative number of runs. However the risks were greater than 1.00 for all three levels, 1.93 for low; 2.22 for medium and 1.22 for high number of runs. It is worth noting that excess colon cancer risk was also reported by Guidotti[13]; Howe and Burch[4]; Schwartz and Grady[31]; and Vena and Fiedler [28], who reported a significant SMR of 1.83. Thus, two studies, one in two out of three subgroups and the other in the population as a whole, have demonstrated relative risks close or equal to a doubling. Although not as easily demonstrable, it may be argued that claims for colon cancer may be justified in the same way as for lung cancer in an individual with a low a priori risk for the disease. We have argued this in the case of a young vegan with no family history of the disease or of polyps, but the claim was not accepted.

Evaluation in Light of Recent Evidence

Table 1 presents the conclusions of the Cancer Care Ontario team, the Industrial Disease Standards Panel and Guidotti, 1995[16].

The experience with firefighters suggests that it is sometimes reasonable to approach knotty adjudication problems by framing the question differently and using collateral evidence to interpret the epidemiological findings. This is particularly true when the purpose is application of epidemiological findings to a legal or adjudicatory process. The Cancer Care Ontario team, notwithstanding the objectives of the study, did not do this. We have done so in this report.

The findings of the Cancer Care Ontario assessment relate only to strength of evidence. They do not address weight of evidence. It is therefore not justified to compare the findings of the Cancer Care Ontario team with the recommendations in the present report, which are based on weight of evidence applying all applicable data and the criteria of balance of evidence that underlies the adjudication process in compensation.

Manitoba, in particular, has taken a responsible position by committing itself to assess the province's experience by conducting a prospective study of cancer incidence and mortality among firefighters to evaluate the policy they have adopted. This commitment in support of occupational epidemiology is a refreshing change from the overall softening of support from the field. Accurate and up-to-date estimates of occupational disease risk, taking into account the relevant time period, are necessary to guide compensation and, even more importantly, to identify opportunities for prevention and hazard control.[3]

The evidence available since 1994 suggests that it is reasonable given the available scientific evidence to adopt a policy of presumption for brain cancer, bladder cancer, kidney cancer, non-Hodgkin lymphoma (lymphatic cancer) and leukemia (haematopoietic cancer) for claims associated with occupation as a firefighter. The presumptions for bladder cancer and kidney cancer are based firmly on a strong suggestion of an excess in the literature. The presumption for testicular cancer is based on recently emerging evidence which demonstrates consistency. The presumption for cancer of the brain is based on the reasonable attribution of the risk to one category of brain cancer based on collateral evidence. The presumption for non-Hodgkin lymphomas and leukemias are based on the inference that within the overall category there are specific disorders for which the evidence suggests an elevated risk but it is not possible

to discern which among several are in excess. A presumption for lung cancer in firefighters who do not smoke is based on the premise that the carcinogenic potential of cigarette smoke and other products of combustion are probably comparable and the risk estimates can therefore be manipulated to "subtract" out the background of smokers' risk.[6]

The application of epidemiology to adjudication and litigation is based on a different set of rules than for scientific investigation. The role of the expert is to give guidance as to the weight of the evidence, not to produce more data or to determine revealed truth through the scientific method. This is particularly important in addressing an individual claim, when generalities based on population data are no longer necessarily valid. As our data resources become more constrained and in many cases outdated, it will become increasingly necessary to interpret the data with greater understanding of the problem rather than relying on rules designed for other purposes, such as the Bradford Hill criteria[6], or standardized numerical processing, such as the approach taken by the Cancer Care Ontario team.

Table 1. Comparison of Conclusions Reached by Various Expert Groups.

Outcome	**CCO, 2004**	**Guidotti, 1995**	**IDSP, 1994**
Criteria:	*Strength of evidence of prospective epidemiological studies*	*Weight of totality of evidence*	*Strength and weight of epidemiological studies*
Lung	No evidence	Association*	No association
Colorectal	Limited**	Association	Association
Bladder	Insufficient	Presumption	Association
Kidney	No evidence	Presumption	Association
Testes	Insufficient	N/A	N/A
Leukemia	Insufficient	Association?	Presumption
NHL	Insufficient	Association?	Presumption
Myeloma	Insufficient	Association?	Presumption?
Brain	Limited	Association	Presumption

* Rebuttable presumption for non-smoking firefighters.

** See report for discussion of colon, rectal and colorectal.

Bibliography

1. Guidotti TL, ed. Emergency and Security Services. Chapter 95 in: ILO Encyclopaedia of Occupational Health and Safety. Geneva, International Labour Organization, 1998.

2. Guidotti TL, Clough V. Occupational health concerns of firefighting. Ann Rev Pub Health 1992; 13:151-171.

3. Guidotti TL Occupational epidemiology. Occupational Medicine 2000; 50(2):141-145.

4. Howe GR, Burch JD. Fire fighters and risk of cancer : An assessment and overview of the epidemiological evidence. Am J Epidemiol 1990; 132:1039-1050.

5. Burnett CA, Halperin WE, Lalich NR, Sestito JP. Mortality among firefighters: a 27 state survey. Am J Ind Med 1994;26:831-833.

6. Guidotti TL, Rose SG. *Science on the Witness Stand: Evaluating Scientific Evidence in Law, Adjudication and Policy.* Beverley Farms MA, OEM Press, 2001.

7. Guidotti TL. Presumption for selected cancers and occupation as a firefighter in Manitoba: the rationale for recent Canadian legislation on presumption. Int J Risk Assess Management 2003:4(2/3):245-259.

8. Deschamps S, Momas I, Festy B. Mortality amongst Paris fire-fighters. Eur J Epidemiol 1995 Dec;11(6):643-6.

9. Guidotti TL, Mortality of urban firefighters in Alberta, 1927 – 1987. Am J Ind Med 1993;23:921-940.

10. Beaumont JJ, Chu GS, Jones JR, Schenker MB, Singleton JA, Piantanida LG, Reiterman M. An Epidemiologic study of cancer and other causes of mortality in San Francisco firefighters. Am J Ind Med. 1991;19:357-372.

11. Hansen ES. A cohort study on the mortality of firefighters. Brit J Ind Med. 1990;47:805-809.

12. L'Abbé KA, Tomlinson GA. Special Report: *Mortality Study of Fire Fighters in Metropolitan Toronto*. Toronto, Ontario Industrial Disease Standards Panel, 1992.

13. Baris D, Garrity TJ, Telles JL, Heineman EF, Olshan A, Hoar Zahm S. Cohort mortality of Philadelphia firefighters. Am J Ind Med 2001;39:463-476.

14. Eliopulos E, Armstrong BK, Spickett JT, Heyworth F. Mortality of fire fighters in Western Australia. Brit J Indust Med 1984;41:183-187.

15. Industrial Disease Standards Panel. Report to the Workers' Compensation Board on Cardiovascular Disease and Cancer Among Firefighters. Toronto, WCB of Ontario, September 1994.

16. Guidotti TL. Occupational mortality among firefighters: assessing the association. J Occup Envir Med 1995;37(12):1348-1356.

17. Demers PA, Heyer N, Rosenstock L. Mortality among firefighters from three Northwestern United States Cities. Br J Ind Med 1992;49:664-670.

18. Heyer N, Weiss NS, Demers P, Rosenstock L. Cohort mortality study of Seattle fire fighters: 1945 – 1983. Am J Ind Med. 1990;17:493-504.

19. Rosenstock L, Demers P, Heyer N, Barnhart S. Mortality experience of fire fighters in the northwest United States. Arbete och Halsa 1998;16:102.

20. Ma F, Lee DJ, Fleming LE, Dosemeci M. Race-specific cancer mortality in US firefighters: 1984 – 1993. J Occup Environ Med 1998; 40(12):1135-1138.

21. Bates MN, Fawcett J, Garrett N, Arnold R, Pearce N, Woodward A. Is testicular cancer an occupational disease of fire fighters? Am J Ind Med 2001;40:263-270.

22. Schottenfeld D, Fraumeni JF. *Cancer Epidemiology and Prevention.* New York, Oxford University Press, 1996.

23. Stang A, Jökel K-H, Baumgardt-Elms C, Ahrens W. Firefighting and risk of testicular cancer: results from a German population-based case-control study. Am J Ind Med 2003;43:291-294.

24. Goldsmith JR, Guidotti TL. Environmental factors in the epidemiology of lymphosarcoma. Pathol Annu. (Part II) 1977;12:411-425.

25. Tatham L, Tolbert P, Kjeldsberg C. Occupational risk factors for subgroups of non-Hodgkin's lymphoma. Epidemiology 1997 ;8(5):551-8

26. Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides (Third Biennial Update), Institute of Medicine. *Veterans and Agent Orange: Update 2002*. Washington DC, National Academy Press, 2003.

27. Guidotti TL, Baser M, Goldsmith JR. Comparing risk estimates from occupational disease monitoring data. Public Health Review 1987; 15:1-27.

28. Vena JE, Fiedler RC. Mortality of a municipal-worker cohort: IV. Firefighters. Am J Ind Med. 1987 (11):671-684.

29. Gerace T.A. Road to a smoke-free fire service for Florida: policies and progress. J Public Health Pol. 1990;11(2):206-217.

30. Guidotti TL. Trends in mortality from COPD in Alberta: back to the future? Can Resp J 1995;2:97-103.

31. New Hampshire Division of Public Health Services, Bureau of Disease Control, 1986. Schwartz E, Grady K. Patterns of occupational in New Hampshire (1975-1985).