Occupational Cancer Research Centre

Ontario Uranium Miners Cohort Study Report

Prepared for:

The Canadian Nuclear Safety Commission

February 2015

Prepared by:

The Occupational Cancer Research Centre,

Cancer Care Ontario

Towards a cancer-free workplace

ACKNOWLEGEMENTS

This update of the Ontario Uranium Miners Cohort was conducted by the Occupational Cancer Research Centre (OCRC) with funding from the Canadian Nuclear Safety Commission. This report was prepared by Garthika Navaranjan, Colin Berriault, and Paul A. Demers from the OCRC and Minh Do, currently with the Public Health Agency of Canada and Paul Villeneuve from Carleton University. Loraine Marrett and John McLaughlin played key roles in the development of this cohort and the initiation of this project. Thanks are due to the staff of the Canadian Nuclear Safety Commission for their scientific comments and suggestions on the report. Special thanks are due to Robert Semenciw of the Public Health Agency of Canada who assisted with Canadian mortality and cancer incidence rates and to Douglas Chambers for his valuable insights and suggestions.

Table of Contents

List of Tables

List of Figures

ACRONYMS AND ABBREVIATIONS

AC	Adenocarcinoma
AECB	Atomic Energy Control Board
AECL	Atomic Energy of Canada Limited
BEIR IV	National Academy of Sciences Committee on the Biological Effects of Ionizing Radiations: Health Risks of Radon and Other Internally Deposited Alpha-Emitters
BEIR VI	National Academy of Sciences Committee on the Biological Effects of Ionizing Radiation
CCO	Cancer Care Ontario
CCDB	Canadian Cancer Database
CCR	Canadian Cancer Registry
CHD	Coronary Heart Disease
CI	Confidence interval
CMDB	Canadian Mortality Database
CNSC	Canadian Nuclear Safety Commission (formerly the AECB)
ERR	Excess relative risk
ETS	Environmental tobacco smoke
GIRLS	Generalized Iterative Record Linkage System
HSTF	Historical Summary Tax File (1984 onward)
ICD-O	International Classification of Diseases for Oncology
ICD	International Classification of Diseases
ICRP	International Commission on Radiological Protection
IR	Ionizing Radiation
LET	Linear energy transfer
LNT	Linear no-threshold
LR	Likelihood ratio test
MeV	Million electron volts
MMF	Mining Master File
NDR	National Dose Registry
OUMC	Ontario Uranium Miners Cohort
PPCC	Parts per cubic centimetre
PPM	Parts per million
RDP	Radon Decay Products or Radon Daughter Progeny
Rn	Radon
RR	Relative risk
SCLC	Small cell lung carcinoma
SIN	Social Insurance Number
SIR	Standardized incidence ratio
SMR	Standardized mortality ratio
SqCC	Squamous cell carcinoma
TSE	Time since last exposure (to radon)
u/mSv	Micro/Milli-Sievert
U_3O_8	Uranium oxide
WL	Working Level
WLM	Working Level Month

EXECUTIVE SUMMARY

This study is an updated analysis of mortality and cancer incidence for a cohort of Ontario uranium miners exposed to radon decay products (RDP). The cohort had been created previously using the Ontario Mining Master File (MMF) (1954-1986) and data from the National Dose Registry (NDR) (1954-2004). For this update the mortality follow-up of the cohort between 1954 and 2007 was expanded by linking to records in the Canadian Mortality Database (CMDB). Similarly cancer incidence from 1969 and 2005 was ascertained by linking to the Canadian Cancer Database (CCDB) at Statistics Canada. Annual exposure to radon, in working level months (WLMs), was available for each cohort member.

This update provides 21 years of additional follow-up from the last full update to examine the risk of lung cancer mortality in Ontario uranium miners. In addition, it examines a larger cohort of Ontario uranium miners through the use of broader entrance criteria and by identifying previous miners through both the MMF and NDR. The larger sample size provides greater precision in estimating lung cancer risk from exposure to RDP. While previous updates of this cohort have only concentrated on the lung cancer mortality experience the present study also examined cancer incidence, as well as examining other cancer sites of interest, such as stomach and leukemia. Non-cancer mortality was also examined. This study also provided the sample size to examine lung cancers by histological groups, including the dose-response relationship associated with the different groups. The relatively lower doses experienced in Ontario, compared to other mine cohorts likewise provided more insight into the risks associated with current day exposures to RDP by uranium miners. This update also provided sufficient follow-up to allow assessment for miners who entered the study after 1970 when more stringent ventilation

practices were introduced. Because two sources of exposure data were available (MMF and NDR), the effect of potential measurement error was also assessed. Exploratory analyses of exposure to gamma radiation dose and cancer and cardiovascular mortality was also conducted through the development of models that estimate an individual's annual exposure to gamma radiation (refer to Appendix A for presentation of exploratory gamma analyses).

External comparisons were made with the Canadian population to derive standardized mortality and incidence ratios for the uranium cohort members. Additional sub-cohort comparisons with the general population were conducted to assess differences in risk for male uranium miners with and without gold mining experience, and for the major Ontario uranium mining regions (Elliot Lake and Bancroft).

Current standard procedures for analyzing radiation epidemiologic studies were utilized; in particular, Poisson regression to fit both relative risk and excess relative risk models for examining the risk associated with varying levels of cumulative exposure to RDP.

The cohort consists of approximately 28,546 male and 413 female uranium miners, who had experience working in Ontario uranium mines for at least one week in the Elliot Lake and Bancroft regions or at Agnew Lake mine between 1954 and 1996. Due to insufficient sample size, women were excluded in the internal analyses examining different doses of exposure, and there were also too few for meaningful comparison with the Canadian population for mortality and cancer incidence.

Compared to Canadian males, increased numbers of deaths for lung cancer (SMR= 1.34, 95% CI: 1.27-1.42), silicosis (SMR=19.68, 95% CI: 14.46-26.18), and accidents, poisoning, or violence (SMR= 1.43, 95% CI: 1.35-1.51) were observed. Lung cancer incidence among male miners was also increased relative to the Canadian population (SIR=1.30, 95% CI: 1.23-1.37). Increased lung cancer mortality and incidence as well as elevations in accidents, poisoning and violence mortality persisted across sub-divisions of the cohort. Silicosis deaths were concentrated among those males who began mining prior to 1960, primarily in the Elliot Lake area, and those who had mined gold previously.

Results suggest a strong dose-response relationship between exposure to RDP and lung cancer mortality and lung cancer incidence. There was about a two-fold increase in the risk of lung cancer mortality (RR= 2.32, 95% CI: 1.72-3.14) and lung cancer incidence (RR=1.89, 95% CI: 1.43-2.50) with a five year lag interval incorporated in the highest cumulative exposure category of >100 WLM. For lung cancer mortality, this relationship was modified by attained age, time since first exposure, time since last exposure, exposure rate, age at first exposure, and dose rate. For lung cancer incidence, this relationship was modified by time since first exposure, time since last exposure and exposure rate.

There were 198 lung cancer deaths observed among miners who started working after 1970. The relative risk among these miners was slightly lower than the entire cohort. However, the small sample size provided limited power to assess the true risk among these miners.

When conducting an analysis of lung cancer cases by morphology the strongest associations with cumulative RDP exposure was seen with squamous ($RR_{>60\ WLM}$=2.03, 95% CI: 1.44-2.86) and

small cell carcinoma ($RR_{>60\ WLM}$= 2.12, 95% CI: 1.29-3.48), both with a five-year lag incorporated. However, smoking may also be an important co-factor to consider in this regard.

Cancer sites other than lung were also examined in this update. In exploring associations between cumulative exposure to radon and cancers of the stomach and leukemia, no excesses or clear dose-response relationships were apparent. Similarly, no clear associations were seen with cardiovascular disease mortality and cumulative radon exposure.

For the sensitivity analysis examining the effect of using different sources of exposure data, overall doses assigned to miners as well as the derived risk estimates were comparable when favoring either the MMF or NDR data for a given miner where doses were provided in both.

In closing, this study was able to build on the understanding of health effects associated with radon exposure among uranium miners by performing an update of the Ontario uranium miners with 21 years of additional follow-up data. The large cohort and national linkage allowed for the sample size to address several gaps in the literature including risks of cancer incidence, associations with specific histological groups and regional analyses of miners. However, limitations of the present study include lack of data on potential confounders and co-exposures of RDP including: smoking status, and silica, arsenic, and diesel exhaust concentrations. Finally, the low doses experienced by these Ontario miners, particularly after better ventilation was introduced, may be similar to the level of exposures experienced by present-day uranium miners. Thus, an analysis of Ontario miners may provide valuable information to aid in the evaluation of current radiation protection practices.

Keywords: radon, cancer, lung cancer, gamma radiation, mining, cohort study

1. INTRODUCTION AND BACKGROUND

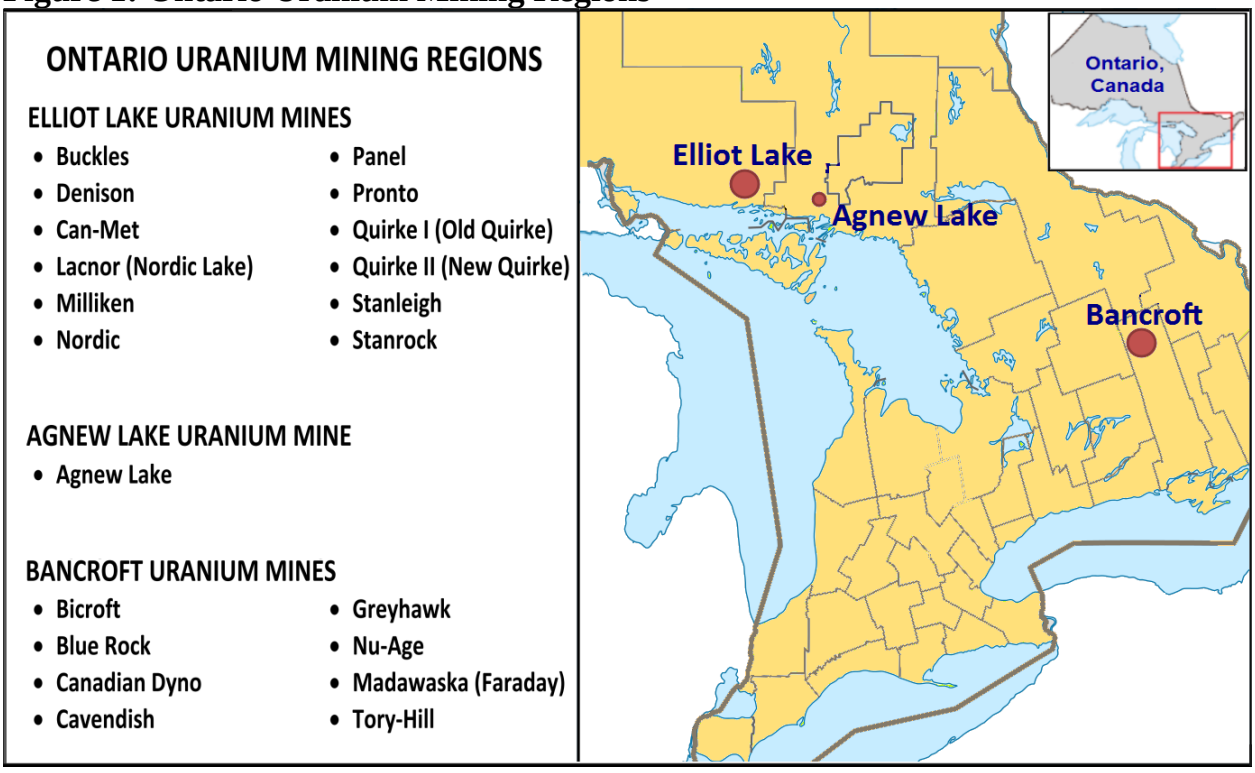
1.1 Canadian Uranium Mining History

Uranium mining has a long history in Canada. These mining activities, which occur predominantly underground, first began in Canada in 1942 at the Port Radium mine in the Northwest Territories. This property was first mined for radium in 1932 (1). With the demand for uranium after World War II, the Eldorado Mining and Refining Company developed the mine at Beaverlodge in 1949 and began full production by 1953 (2). The Beaverlodge mine continued operation until June 1982 (3). Aside from the mines in the Elliot Lake, Bancroft, and Sudbury District regions of Ontario, the Beaverlodge mine operated contemporaneously with nine other uranium mines in Northern Saskatchewan, and one in the Northwest Territories. For an illustration of uranium mines and mining regions past and present across Canada refer to Appendix C (4).

Miners in Canada have also been exposed to radon decay products from calcium fluoride (fluorspar) mining in the St. Lawrence Newfoundland region from 1933 with an open pit and from 1936 to 1990 underground (5, 6). The mines originally closed in 1978 but were re-opened briefly in the mid-1980s. Concentrations of radon gas in the mines were very high (i.e., 0.4-190 WL) due to contamination from ground water seepage, in many cases leading to higher exposures than those found in most Canadian uranium mines during the pre-1960 installation of mechanical ventilation (6, 7). Following introduction of mechanical ventilation levels of radon gas fell to a mean of 0.3 WL from 1961 to 1967 (8). Observed mean cumulative radon dose among members of this cohort was 378 WLM (6).

In Ontario, sufficient ore grades of uranium for mining were found in the Elliot Lake, and Bancroft areas, as well as Agnew Lake and to a lesser degree Nipissing Lake regions (9). Uranium mining in the province started in the mid-1950's in the Elliott Lake and Bancroft areas, beginning with Pronto mine in the Elliot Lake region. Uranium production developed rapidly beginning in 1954 with 500 development miners, reaching a peak during 1957 to 1960 with 10,000 miners, and declining just as rapidly after 1960 with less than 1,000 miners by the mid-1960s (9-11). The sudden market collapse for Ontario uranium oxide ore reduced the number of mines in the province from a dozen operating mines in 1960 to two by 1975 (11). There was a uranium mining resurgence in Ontario due to power generation requirements in the late 1970s and 1980s, but this involved mainly the Elliot Lake mining region as only Faraday was reactivated in Bancroft in 1978 and closed again permanently by 1982. Only Denison and Stanleigh mines remained in operation by the 1990s, finally ceasing operations , in 1992 and 1996 respectively due to decreased demand and reduced profitability (10, 12, 13). Figure 1 shows the geographical locations of individual Ontario uranium mines within the three mining regions of Elliott Lake, Agnew Lake, and Bancroft area.

Figure 1: Ontario Uranium Mining Regions



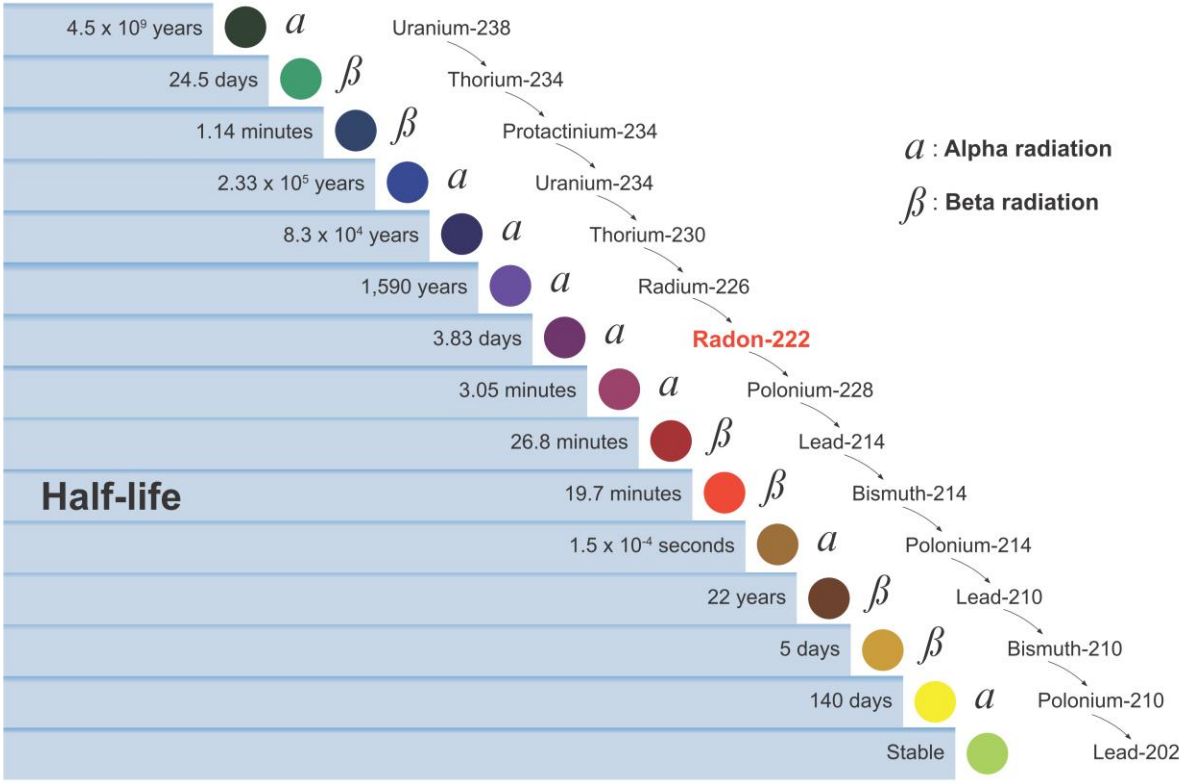
Types of ore present in Ontario uranium mines, which release radioactive isotopes include uranium (as U3O8) in the Elliot lake, Agnew Lake, and Bancroft area mines, and thorium at mineable concentrations in the Elliot Lake and Agnew Lake mines (9, 10). Likewise, for a period of time, rare earth minerals were extracted at Denison mine which would have resulted in thorium exposures for workers at that site (12, 14).

1.2 Uranium Mine Exposures and Health Effects

For many years, radon has been recognized as a hazard to underground miners (15-19). Epidemiological studies of underground miners provided the basis for estimating the risk from exposure to radon though it is also recognized that domestic exposure to radon carries a risk. The potential for radiation to induce malignant cell transformations exists due to the decay products of radioactive materials such as uranium, wherein particles ejected from atoms may come into close proximity with cells (20, 21). Malignant damage occurs when the ejected particles deposit energy as they pass through the cell and the relationship between the amount of energy deposited and the track length over which it is deposited is the linear energy transfer (LET) (22). High LET radiation has more potential for inducing cell damage than low LET radiation. ^{222}Rn (radon) is a noble radioactive gas that arises from the radioactive decay chain of ^{238}U (uranium), while a different isotope of radon, ^{220}Rn (thoron) arises from the radioactive decay chain of ^{232}Th (thorium) (15, 23). Radon decays with a half-life of 3.82 days into a series of isotopes or radon decay products (RDP) such as Polonium-218 through emission of alpha particles. Refer to Figure 2 for an example of the Uranium-238 decay chain (24). The risk of lung cancer due to radon exposure is caused by radon decay products (RDPs), which are suspended in air when radon gas is present, and attach to dust particles or the surface of solids. Whether attached or unattached RDPs may be inhaled and deposited in the lungs where they emit alpha radiation (21). Due to their relatively short half-lives, RDPs decay for the most part, while deposited in the lung (21, 24). Although the radiation can also be absorbed by the nasal cavity, unlike the lungs the nasal mucosal layer provides some protection (8). Damage results when these radioactive elements come into close proximity to lung tissue, particularly in the larger airways of the lung, where they have a propensity to settle out. This is supported by evidence that miners exposed to radon

have a higher ratio of central to peripheral lung tumours than non-miner smokers, whose major carcinogen (tobacco smoke) tends to settle out and cause cancer in more peripheral airways (21, 25).

Figure 2: Uranium-238 Decay Chain



Studies of smoking and non-smoking miners show that exposure to radon decay products carries a substantially enhanced risk of lung cancer as do radon concentrations in indoor air (6, 26-34). Non-smokers exposed to elevated levels of radon over a lifetime are said to have a 1 in 20 chance of developing lung cancer, which increases to 1 in 3 for smokers exposed to similar RDP levels (24, 26). A number of case-control studies have examined the risk of concurrent exposure of uranium miners to radon and smoking (22, 26, 28, 35). The majority of case-control studies over the past 30 years have observed a greater than additive but less than multiplicative relationship between RDP exposure and smoking status (27, 30, 31, 34, 36, 37). The majority of

cohort studies with smoking data have found an additive interaction between the two exposures, with some studies observing something between an additive and multiplicative risk model (22, 35).

Inverse dose-rate effect

The term "inverse dose-rate effect" is used to describe that a given dose of radiation will be more effective at causing carcinogenesis if it is delivered over a protracted period of time rather than as an acute dose (22, 38). Therefore, the theory proposes that a lower dose rate is more effective at cancer causation, due to cells being more vulnerable to damage during specific periods of their cycle (21). Only a small proportion of cells may be at a vulnerable stage during an acute dose but a dose rate effect is only probable when the total dose is sufficient for multiple traversals of individual cell nuclei (i.e., multiple cell hits by alpha particles) (16, 21). Studies involving underground miners have observed a diminution of the inverse dose-rate effect below 50 WLM exposure (16). In the residential setting, the exposure may be so low (typically 15-20 WLM for a lifetime) that they fall below the threshold for the inverse-dose-rate effect (16, 21, 39).

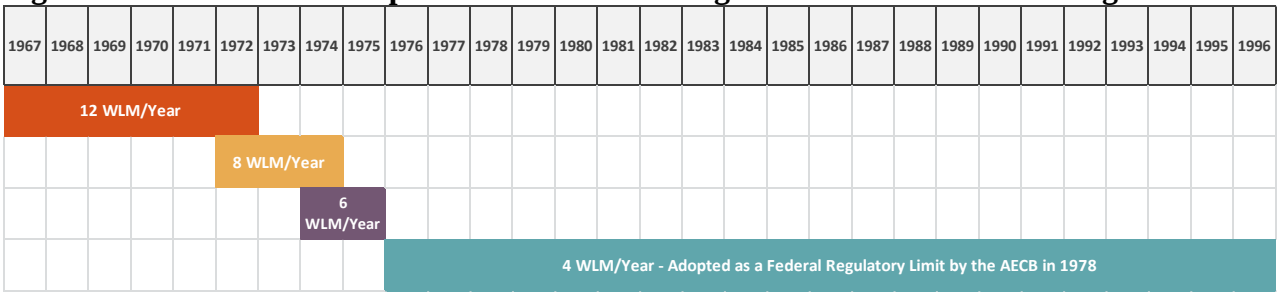
Linear no-threshold theory

This theory was proposed as a model for relative risk for lung cancer mortality associated with radon exposure. In essence the theory holds that relative risk of lung cancer is linearly related to radon exposure (20). The BEIR IV (20) posited that there is no threshold below which the risk of lung cancer associated with exposure to radon is zero (21, 40). A further update of the model observed an Excess Relative Risk (ERR) related linearly with past radon exposure (21), and BEIR VII supports the application of the model at low doses (38).

1.3 Ontario Radon Exposure Regulation

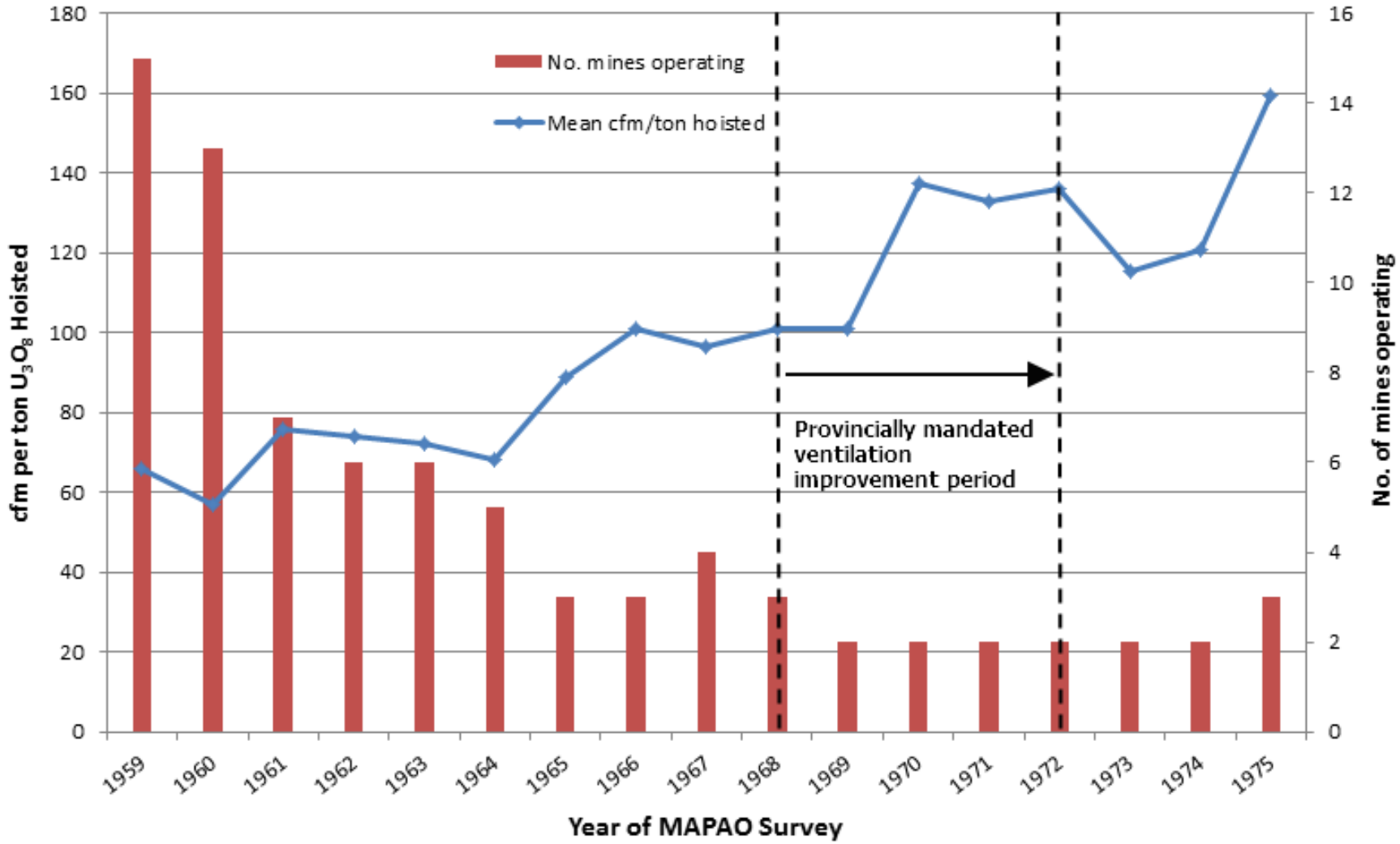
Regulation of radon decay products (RDP) exposure in Ontario uranium mines began in the early 1950's as a guideline (4 WLM annually) suggested by the Atomic Energy Control Board (AECB), which had no regulatory enforcement authority (9). By 1967 the AECB was given some regulatory authority, but concerned itself primarily with environmental effects of uranium mining leaving occupational exposure limits to be instituted by the provinces. Following consultations the Ontario Department of Mines instituted a limit of 12 WLM annually for RDP exposure in uranium mines, which was further adjusted over time (9, 11, 12). Regulatory authority rested primarily with provincial agencies with a 4 annual WLMs permissible limit set by 1976 and adopted by the AECB which opted to exert more regulatory authority following the Ontario Ham Commission report and the Hydro Affairs Committee Hearings (refer to Figure 3 following) (9). A number of studies have suggested that 1967 mandated changes in ventilation requirements and radon exposure regulation by the Ontario Department of Mines, which gave mining companies until 1972 for ventilation upgrades and 1975 for radon exposure limit compliance would have resulted in decreased radon decay product exposures (9-11, 41, 42). Refer to Figure 4 for first period of the Mines Accident Prevention Association (MAPAO) survey for mean ventilation airflow results in Ontario uranium mines (results are in mean airflow cubic feet per minute by ton of U_3O_8 hoisted per day) (11).

Figure 3: Ontario Radon Exposure Standards during Provincial Uranium Mining Period



WLM/Year = Cumulative annual working level months exposure limit before being reassigned from underground (9, 12, 42, 43)

Figure 4: Ontario Uranium Mines Mean Annual Total Mine Ventilation (cfm/ton hoisted per day (thousands)



MAPAO = Mines Accident Prevention Association of Ontario **cfm** = cubic feet per minute
Total mine ventilation presents only results from first survey periods (i.e., March)
Adapted from the Report of the Royal Commission on the Health and Safety of Workers in Mines, 1976

2. URANIUM MINING COHORT STUDIES OVERVIEW

Table 1: International Cohorts of Uranium Miners

Study Cohort	Records for Cohort Assembly	Locations and Operating Periods	No. in Cohort	Follow-up Outcome Measures	Radiation Measures Availability*	Inclusion Criteria	Record Linkage/ Ascertainment
USA							
Colorado (44)	Health screening volunteers (1950-1960) & administrative records	Colorado Plateau (1936-1968)	Males 4,137	1950-2005 Mortality	Radon: 1949 γ-ray: na	Employed 1+ months; Alive start of follow-up; Health screening (1950-60)	**Causes of death**: 1) National Death Index (1979-2005); 2) Social Security Administration Death Master File **Vital ascertainment**: 1) Company records; 2) National Death Index; 3) Social Security Administration Death Master File **Reference Population:** American
New Mexico (45)	Company administrative records	Grants area (Laguna, Ambrosia Lake, and Church Rock areas; 1955-1990)	Males & Females 2,745	1979-2005 Mortality	Radon: 1950s γ-ray: na	Employed 6+ months; Alive start of follow-up	**Causes of death:** 1) National Death Index (1979-2005); 2) Social Security Administration Death Master File **Vital ascertainment:** 1) National Death Index; 2) Social Security Administration Death Master File; 3) Credit bureaus; 4) Comserv **Reference Population:** American
Canada							
Eldorado (46, 47)	Eldorado Nuclear administrative records & National Dose Registry	Beaverlodge (SK; 1950-1980), Port Radium (NWT; 1942-1980) mine sites, and Port Hope Refinery (1932-1960)	Males 16,236 Females 1,424	1950-1999 Mortality; 1969-1999 Cancer Incidence	Radon: 1954; 1945; na γ-ray: 1950s; 1950s; 1940s	Employed at Eldorado; Alive start of follow-up; Age at entry: 15-75 years	**Linkage:** Statistics Canada (National) **Causes of death:** Canadian Mortality Database (1950-1999); **Cancer incidence:** Canadian Cancer Registry (1969-1999); **Vital ascertainment:** Historical Summary Tax File (1984-1999); **Reference Population:** Canadian

Table 1: International Cohorts of Uranium Miners continued

Study Cohort	Records for Cohort Assembly	Locations and Operating Periods	No. in Cohort	Follow-up Outcome Measures	Radiation Measures Availability*	Inclusion Criteria	Record Linkage/ Ascertainment
Canada							
Newfoundland (6, 7)	Administrative records of two mining companies	St. Lawrence area (1933-1978)	Males 2,070:	1950-2001 Mortality	Radon: 1960 γ-ray: na	Employed during operating period; Alive start of follow-up	**Linkage:** Statistics Canada (National) **Causes of death:** Canadian Mortality Database (1950-2001); **Vital ascertainment:** Historical Summary Tax File (1984-2001); **Reference Population:** Newfoundland
Ontario	Mining Master File & the National Dose Registry	Elliot Lake (1954-1996), and Bancroft areas (1954-1982)	Males 28,546 Females 413	1954-2007 Mortality; 1969-2005 Cancer Incidence	Radon: 1954 γ-ray: 1981	Employed 1+ weeks; Alive start of follow-up; Age at entry: 15-65 years	**Linkage:** Statistics Canada (National) **Causes of death:** Canadian Mortality Database (1950-2007); **Cancer incidence:** Canadian Cancer Registry (1969-2005); **Vital ascertainment**: Historical Summary Tax File (1984-2007); **Reference Population:** Canadian
Europe							
Czech Republic (48, 49)	Company administrative records	Jachymov area (West Bohemia; 1948-1965), and Pribam mines (Central Bohemia; 1968-1974)	Males 9,978	1952-2010 Mortality	Radon: 1949 γ-ray: na	Employed 1+ years; Alive start of follow-up	**Linkage**: Institute of Health Information and Statistics (ÚZIS) **Causes of death**: 1) Local death registries (1952-1981); 2) Institute of Health Information and Statistics (1982-2010) **Vital status:** Czech Population Registry (1952-2010); **Reference Population:** Czech & Slovak
France (17, 50)	CEA & AREVA administrative records	Massif Central, Vendee, and Herault areas (1946-1990)	Males 5,086	1946-2007 Mortality	Radon: 1953 γ-ray: 1956	Employed 1+ year; Alive start of follow-up	**Vital status:** national vital status registry (1946-2007) **Causes of death:** 1) AREVA medical archives (1946-1967); 2) national registry of medical (1968–2007) **Reference Population:** French

Table 1: International Cohorts of Uranium Miners continued

Study Cohort	Records for Cohort Assembly	Locations and Operating Periods	No. in Cohort	Follow-up Outcome Measures	Radiation Measures Availability*	Inclusion Criteria	Record Linkage/ Ascertainment
Europe							
Germany (51-54)	Wismut Co. administrative records	Thuringia, and Saxony areas (1946-1990)	Males 58,982	1946-2008 Mortality	Radon: 1954 γ-ray: 1963	Employed 6+ months; Alive start of follow-up	**Vital status:** Local registries and Public Health offices archives **Causes of death:** Wismut Co. pathology archive (1946-2008) **Reference Population:** German
Australia							
Radium Hill (55)	Radium Hill administrative records	South Australia (1952-1962)	Males 2,521 Females 53	1952-1987 Mortality	Radon: 1954 γ-ray: na	Hourly employees; Employed 1952-1961;	**Vital status:** 1) Australian death record search (1960-1987); 2) South Australia death record search (1952-1959) **Causes of death:** Death certificates **Reference Population:** Australian

*Availability of radiation measures represents the year or period when quantitative measurements of radon,RDP or γ were first performed

2.1 International Studies

In order to assess the risks of occupational exposure to radon and other forms of radiation in mines, a number of uranium miner cohorts have been assembled and studied. Table 1 lists the major uranium miner cohorts and provides some basic characteristics for each cohort. A description of the results from the most recent updates for each major cohort is presented below.

The Colorado Plateau uranium cohort contained 4,137 miners, who experienced some of the highest levels of radon exposure (22). The most recent follow-up added 15 years of mortality follow-up through December 31, 2005 (44). An excess of lung cancer mortality was observed in both white miners (SMR=4.96; 95% CI: 4.55-5.39) and American Indian miner (SMR=3.18; 95% CI: 2.54-4.07). An excess in stomach cancer was observed among American Indian miners (SMR: 1.92; 95% CI: 1.02-3.28), but not for white miners (SMR: 1.33; 95% CI: 0.78-2.13). A dose-response relationship was also observed with cumulative exposure to radon across all categories of cumulative exposure with a standardized rate ratio (SRR) of 2.4 (95% CI: 1.6-3.5) in the 120-<400 WLM category and SRR=9.2 (95% CI: 6.3-13) observed in the highest category of $\geq$ 1000 WLM for all miners combined. The study also examined interaction between radon and smoking on lung cancer and found it to be greater than additive, but less than multiplicative.

The New Mexico cohort examined mortality among 2,745 mine and mill employees of which 1,745 were miners. Among the underground miners a two-fold excess in the number of lung cancer deaths was observed (SMR=2.17, 95% CI:1.75-2.65). Other excess were observed for non-malignant respiratory disease (including bronchitis, influenza, and others) (SMR=1.64, 95%

CI:1.23-2.13), cirrhosis of the liver (SMR=1.79, 95% CI: 1.06-2.83), accidents (SMR=1.5, 95% CI:1.02-2.13) and suicide (SMR=2.06, 95% CI:1.28-3.15)(45).

In their most recent update, the Czech cohort extended follow-up by 10 years for 9,978 miners with 1,141 lung cancer deaths observed (48). The crude excess relative risk per WLM was 0.0097 (90% CI: 0.0074–0.0127). The SMR observed for lung cancer mortality was 3.47 (95% CI: 3.27-3.68). The study also examined three key modifying factors: time since exposure, age at exposure and exposure rate. The strongest effect was seen for time since exposure ($p<0.0001$), then exposure rate ($p=0.0002$) and age at first exposure ($p=0.0004$) where the risk decreased with an increase in years for each modifying factor.

The French cohort consisted of 5,086 miners and was updated with follow-up through 2007 by an additional eight years of follow up with 211 lung cancer deaths (50). An overall excess of lung cancer mortality was observed among the miners (SMR=1.34, 95% CI: 1.16-1.53) as well as an excess number of deaths for kidney cancer (SMR=1.60; 95% CI: 1.03–2.39) and silicosis (SMR= 6.12, 95% CI: 4.13-8.74). An association was observed between cumulative exposure and lung cancer death (ERR/100 WLM = 0.71, 95% CI: 0.31-1.30) and cerebrovascular disease (ERR/100 WLM= 0.41, 95% CI: 0.04-1.03) (50).

The German cohort remains the largest cohort of uranium miners with approximately 59,000 miners and just over 3,000 lung cancer deaths. A recent review of all the German Wismut cohort studies highlighted the most important finding as a dose-response relationship seen for lung cancer and cumulative radon exposure, as well as from cumulative silica dust exposure(52). In

the most recent update the ERR per 100 WLM for lung cancer was 0.20 (95% CI: 0.17-0.22). Other sites with increased risk were stomach cancer (ERR/100 WLM= 0.022 (95% CI: 0.001-0.042) and extra-pulmonary cancers (ERR/100 WLM= 0.014, 95% CI: 0.006-0.023). This study also examined the potential confounding effects of important co-exposures including external gamma radiation, long-lived radionuclides, arsenic, fine dust and silica dust and found that these co-exposures only had minor effects on the ERR/WLM for lung cancer (52). Smoking data was only available for some members of the cohort, and was not found to be a confounder of the lung cancer and radon association. Further assessment of smoking, with data combined with two other European studies revealed a greater than additive and less than multiplicative interaction between radon exposure and smoking.

The Radium Hill uranium miner's cohort of Australia contained 2,574 miners. Similar to other studies, an excess of lung cancer deaths was observed (SMR: 1.94 (95%: 1.42-2.45) in the cohort (55). For analyses examining cumulative radon exposure, a two-fold increase in the risk of lung cancer was observed among underground workers in the 10-40 WLM category (RR=2.2, 95% CI: 1.0-4.7) compared to surface workers. For underground miners with exposures >40 WLM the rate ratio increased five-fold (RR= 5.2, 95% CI: 1.8-15.1) compared to surface workers (55).

2.2 Canadian Studies

The most recent follow-up for the Eldorado cohort (i.e., Beaverlodge and Port Radium mines and the Port Hope refinery) was extended from 1950 to 1999 for 17,660 uranium workers (46). The new analyses included both mortality and cancer incidence outcomes with lung cancer significant excesses in both mortality (SMR=1.31, P<0.001) and incidence (SIR=1.23, P<0.001).

Linear increases in lung cancer ERR per 100 WLM were observed for mortality (ERR=0.55, 95% CI: 0.37- 0.78) and incidence (ERR=0.55, 95% CI: 0.37-0.81), consistent with contemporary risk estimates and the past pooled study of 11 mining cohorts (46, 56). No cancer sites or causes of death were associated with γ-ray doses, with a mean dose of 52.2 millisieverts (mSv) for males. However, there was a non-significant increase in chronic lymphocytic leukemia (CLL) ERR per Sievert (Sv) γ-ray dose observed (ERR=7.52/Sv, 95% CI: <0-57.1). Estimates were similar in magnitude to those of the BEIR VI model with agreement observed for time since exposure and exposure rate, while age at exposure differed (22, 46).

The Newfoundland fluorspar (calcium fluoride) miners had relatively high RDP exposures due to ground water contamination (mean cumulative WLM = 378). These miners were employed from the 1933 to 1978, with the most recent follow-up available for 1950-2001 for 1,742 miners and 328 mill workers with a total of 191 lung cancer deaths (6, 8). Relative to the Newfoundland population excesses in mortality were observed for lung cancer (SMR=3.09, 95% CI: 2.66-3.56), silicosis (SMR= 38.9, 95% CI: 15.58-80.13) and accidents, poisoning, and violence (SMR=1.58, 95% CI: 1.24-1.98). There was also an inverse dose-rate effect observed for ERR/WLM (6). Smoking surveys over the period of 1966 to 2003 were available for approximately half of the cohort, which were used to investigate the interaction of smoking and radon exposure. While no difference in risk was observed between ever and never smokers, there was a significant excess relative risk per working level month of exposure (ERR/WLM) with increasing number of cigarettes smoked daily. The small number of lung cancer deaths precluded distinguishing between additive and multiplicative effects (6).

2.3 Ontario Studies

The earliest evidence of increased risk of lung cancer in Ontario uranium miners was provided in the Muller report in 1974 (57). The Report of the Royal Commission on the Health and Safety of Workers in Mines was spurred largely by outcry over the findings of Muller's earlier report and provided a more comprehensive examination of lung cancer in Ontario uranium mines which subsequently resulted in the epidemiological cohort studies of Muller and the Workers' Compensation Board Occupational Disease Panel. Several cohort updates were performed with varying inclusion criteria for the nearly 27,000 ever Ontario uranium miners derived from the Mining Master File (MMF: refer to description in section 4. Methodology) (11, 14, 34, 42, 57-59). The most recent update by Kusiak et al. (14) observed an average of 15.1 person-years at risk per man and a mean exposure in the range of 40-90 WLMs and the expected association with lung cancer (14). The study also observed a time since exposure effect where the risk of lung cancer decreased with increasing time since exposure and attained age (14, 60). The effect was subsequently verified by others including Lubin et al.(16, 32, 39), BEIR VI (22) and BEIR VII (38).

Table 2: Overview of Previous Ontario Uranium Miner Cohort Studies

(REF.) STUDY YEAR	FOLLOW-UP PERIOD	COHORT SIZE[@]	LUNG CANCER SMR (95% CI)	RECORD LINKAGE
(27) 1974	1955-72	8,649	3.13 (2.75-4.16)	Provincial – Death certificate search
(11) 1976	1955-74	~18,000	1.80 (1.43-2.23)	National – Linkage
(24,28) 1983	1955-77	15,984	1.81 (1.50-2.14)	National – Linkage with CMDB
(29) 1989	1955-81	14,877	1.70 (1.46-1.97)	National – Linkage with CMDB
(19) 1993	1955-86	21,346	1.71 (1.52-1.91)	National – Linkage with CMDB

CMDB – Canadian Mortality Database All cohorts were assembled from MMF data
Differences in the cohort size shown are due to varying inclusion criteria used between updates

A number of studies in Ontario mines have identified other potential confounding lung cancer risk factors including: silica dust, diesel exhaust, and multiple ore mining experience (12, 14, 42, 59, 61).

The most recent study of cancer in the Ontario uranium miners was performed by Do and colleagues from Cancer Care Ontario (62). The study focused only on gastrointestinal cancers. The cohort was created by combining data from the MMF with data extracted from the National Dose Registry, resulting in the identification of more uranium miners, as well as the addition of more work history and exposure data for miners originally in the MMF. The present study uses the cohort of Ontario uranium miners created by Do and colleagues.

3. RESEARCH OBJECTIVES

The main goal of this project is to update the estimates of lung cancer mortality for Ontario uranium miners exposed to radon daughters. The last national update of mortality for this cohort was for the period 1955-1986, which was over 25 years ago. This study includes additional mortality follow-up to the end of 2007 and cancer incidence follow-up from 1969 to 2005, which provides more power to assess the risks of lung cancer mortality. The extended follow up will also allow greater assessment for miners who entered the study later since cancer has a long latency period. The present study also contains the addition of work histories up to 1996 and thus covers the entire period of uranium mining in Ontario. While past updates have been concerned primarily with lung cancer mortality, this study also aims to examine lung cancer incidence, other cancers sites and non-cancer mortality for Ontario uranium miners from exposure to radon daughters. Likewise a novel exploratory analysis of gamma radiation exposure and dose as they relate to cancer incidence, mortality and non-cancer mortality will be conducted through the development of models for an individual's estimated annual gamma exposure (refer to Appendix A for preliminary gamma dose analyses).

The specific research objectives of this study are:

1. To update estimates of the exposure to RDP and lung cancer mortality (for follow-up period 1954-2007)
2. To examine exposure to RDP among modern miners, at relatively low doses starting mid-to-late 1970s, when improved ventilation systems were introduced
3. To assess exposure to RDP and lung cancer incidence (for follow-up period 1969-2005)
4. To evaluate the impact of modifying factors' (attained age, time since exposure and exposure rate) on the RDP and lung cancer risk relationship

5. To compare results from the lung cancer mortality and incidence analyses
6. To conduct an exploratory analysis of exposure to gamma radiation dose and cancer incidence and mortality, and non-cancer mortality (refer to Appendix A for exploratory analyses)
7. To conduct an exploratory analyses of RDP exposure and cancer incidence and mortality for cancers other than lung
8. To conduct an exploratory analyses of RDP exposure and non-cancer mortality
9. To compare the rates for mortality (SMRs) and cancer incidence (SIRs) among the miners with those for the general population
10. To perform a sensitivity analysis of the effect of measurement error in exposure estimates on the corresponding risk estimates. (refer to Appendix B for assessment of the sources of exposure uncertainty)
11. To perform the histological and morphological analysis of the lung cancer cases.

The Canadian Nuclear Safety Commission (CNSC) obtained ethical approval for this study from the Health Canada's Research Ethics Board (REB 2007-0015), and data access agreements from Ontario Workplace Safety and Insurance Board (WSIB) and Health Canada for the use of the Ontario Mining Master File (MMF) and the National Dose Registry (NDR), respectively. The CNSC also obtained approval from Statistics Canada's Policy Committee and the Provincial/Territorial vital statistics registrars and cancer incidence registries to link the cohort to the Historical Summary Tax File (HSTF), Canadian Mortality Database (CMDB) and Canadian Cancer Database (CCDB). The Occupational Cancer Research Centre received ethics approval from the University of

Toronto to conduct the analyses and maintains approval with the Workplace Safety and Insurance Board (WSIB) for use of the Mining Master File.

4. METHODOLOGY

The present study uses the cohort of Ontario uranium miners created by Do and colleagues (13, 62). The cohort included all miners who worked for at least one week in an Ontario uranium mine between 1954 and 1996 based on data in Ontario's Mining Master File (MMF) and data from the National Dose Registry (NDR) (63, 64).

The Ontario Mining Master File (MMF) contains work history and radon exposure data for hard rock miners, who worked in Ontario during the period of 1928 to 1986. The Ontario Silicosis Act resulted in the creation of the MMF in 1928 (14, 63, 65, 66), which required all miners working in Ontario to have annual medical exams with chest X-rays to be certified as fit for underground mining work. The focus of the early clinics was detecting early signs of silicosis and other non-malignant respiratory diseases (59, 63). During annual exams employment histories were collected for information since the last exam by the Government of Ontario Ministry of Health. Beginning in 1951 files of workers with radiological signs of silicosis or tuberculosis began to be coded onto punch cards (12, 59, 63). In 1955 this was extended so that all workers participating in the clinics with at least 60 months of cumulative mining experience or two weeks of uranium mining experience were coded, regardless of chest x-ray status. The punch card data was later transferred to magnetic tapes during the late 1960's to early 1970's period (57). The resulting database of underground miners became known as the Mining Master File (MMF) maintained and updated annually by the Ontario Worker's Compensation Board (currently the Workplace Safety and Insurance Board or WSIB) until 1987 (12, 42). The MMF has detailed work histories for each miner including all mines where employed, job type, location and ore mined for each year. For uranium miners, annual radon dose information was

available from 1954 to 1986, but no gamma measures were available. The inclusion criteria for this cohort were male miners from the MMF who worked in a uranium mine in Ontario between 1954 to 1986 for at least six months (62). This cohort of miners from the MMF was then expanded by identifying uranium miners from the NDR.

The National Dose Registry (NDR), created in 1951, is a mandatory registry maintained by the Radiation Protection Bureau of Health Canada. Radiation dose information on all monitored workers in Canada (e.g. dentists, X-ray technologists, reactor workers, uranium miners) is entered into this centralized record-keeping system (64, 67). The registry contains detailed radiation history records for workers beginning in the 1940's collected from the National Dosimetry Services (NDS), as well as, data submitted by nuclear power generating stations, Atomic Energy of Canada Ltd. (AECL), private dosimeter processing companies, and uranium mines (64, 67-69). In 1951 the NDS began collecting data from Canadian radiation workers, excluding Ontario uranium miners. The Atomic Energy Control Act (AECA) in 1978 required Ontario uranium mining companies to submit past (i.e., 1952 to 1977) and ongoing radiation exposure, and work history records (e.g., radon dose, year, mine, and job) of uranium miners to the NDR (64, 70, 71). Additionally, the NDR contains gamma doses for Ontario uranium miners from 1981 when personal thermoluminescent dosimeters (TLDs) were provided by the NDS (64, 71). For inclusion into this cohort individuals had to have worked in an Ontario uranium mine between 1954 and 1996 with complete work history and radiation exposure (such as radon and gamma) information. Of those employed during the inclusion period of Ontario uranium mine operation (1954-1996), some had continued employment in radiation exposed industries (e.g.,

Saskatchewan uranium mines, mine decommissioning, etc.), which resulted in NDR work histories and radiation exposure records extending to 2004.

Workers with insufficient work and exposure information for analysis were excluded from the cohort (Figure 5). First, duplicate miner records were excluded. Miners with missing date of birth were excluded due to the inability to calculate elements required for analyses (e.g., age at entry, etc.). Moreover, the ability to do valid record linkage for those with missing date of birth was also questionable. Exclusions based on invalid age at first employment included those younger than 15 or older than 65 years at entry into the study. Individuals over 65 years of age at entry into the study were not linked to a death record, and were considered to be alive until the end of our follow-up, causing them to contribute person-years beyond what would be expected based on their advanced age of entry. Individuals whose only source of exposure information was NDR records without exact dates and exposure presented in ranges (referred to as spanner records) were excluded because without exact date of exposure, key variables such as duration of exposure and date of entry into the study cannot be calculated. Individuals whose start of employment was after 1996 were excluded as that was the last year a uranium mine operated in Ontario. Thus, these individuals hired after 1996 may have been involved with the decommissioning of the mines, but were not true miners. The NDR collected information on a variety of workers, including miners. To ensure that only true miners were included in our cohort, individuals with records only in the NDR who did not have at least one uranium mining record were excluded. Lastly, miners with invalid dates were excluded since accurate person-years could not be calculated.

Radon exposure assessment

Ontario uranium miners' exposure to radon decay products were estimated mainly using stationary area sampling. Prior to 1958, annual average radon levels were estimated based on mine-specific extrapolations by mining engineers (22, 63). The extrapolation technique took into consideration the amount produced, ventilation practices and dust counts available for that mine (59). After 1958, measurements of radon decay products were taken in mines by mine operators and reported to government authorities quarterly (11). Stationary samples were taken in different areas of the mines including in headings, stopes, raises and travelways. The percentage of time spent in work areas and travelways were used to assign individual exposures to miners based on their length of employment (20). From 1968 radon dose assignment became more systematic with detailed work histories collected for each individual on duration of task in specific locations. These were combined with extensive and consistent area sampling to assign estimates of personal exposures (59, 63).

Annual radon doses were provided in the NDR for the period 1954-2004 and in the MMF from 1954-1986. Workers found only in the MMF had their radon doses taken from the MMF. Similarly if a worker was found only in the NDR then their radon doses were taken from the NDR. In some cases individuals had doses in both sources. Where there were doses provided in both the NDR and MMF for a given year, the NDR measurement was used as the best radon concentration, as NDR data tended to be more complete.

Record Linkage and Mortality Ascertainment

The cohort file was first linked to the Historic Summary Tax File (HSTF) to verify and update personal identifiers to aid with the linkage to the CMDB and CCDB, as well as validate the mortality linkages made with mortality records. Cohort mortality was ascertained by linkage of personal identifiers to the Canadian Mortality Database (CMDB) from 1954 to 2007 and cancer incidence was ascertained by linking to the Canadian Cancer Database (CCDB) from 1969 to 2005. The mortality and incidence linkages were performed by Statistics Canada using a probabilistic linking program (Generalized Iterative Record Linkage System) (72). Underlying causes of death were coded according to the version of the International Classification of Diseases (ICD) that was in effect at the time of death. Incident cancer cases were coded using ICD-9 for diagnoses before 1992 and ICD-0-3 for diagnoses 1992 and onward. Linkages underwent manual review by Statistics Canada and Canadian Nuclear Safety Commission employees and due to the assumed completeness of the databases those not found were assumed to be alive. The accuracy of the GIRLS mortality record linkage to the CMDB has been tested and the probability of identifying deceased cohort members was 98.2% (95% CI: 97.5-98.7%), while the probability of identifying live cohort members was 100% (73).

4.1 Statistical Analysis

4.1.1 External Cohort Comparison

The mortality and cancer incidence experience of this cohort was compared to that of the general Canadian population. National rates of cause-specific mortality and cancer incidence by sex, five-year age and five-year calendar periods were obtained from the Public Health Agency of Canada. Comparisons with the general population were conducted using traditional techniques

for deriving standardized ratios (74, 75). Standardized mortality and incidence ratios and their 95% confidence intervals (CI) were calculated assuming deaths and cancers followed a Poisson distribution. All tests of significance were two-tailed (74).

Previous studies of the Ontario uranium cohort have observed increased lung cancer mortality risks for those who also had gold mining experience (14, 59, 63). Potential exposure differences between the Elliot Lake and Bancroft uranium mining regions have also been identified. Ore in the Elliot Lake region contains more quartz with known silicosis risks, while shrinkage stope mining methods common to Bancroft mines were found to result in higher mean radon decay product concentrations by stationary samplers due to leftover muck in the stopes, etc. (41, 42, 61). In an effort to look at co-exposures, we performed additional sub-cohort analyses examining miners with and without a previous history of gold mining separately, as well as sub-cohorts based on Ontario uranium mining geographic region (i.e., Elliot Lake and Bancroft) due to the possible differences in co-exposures that may have occurred.

4.1.2 Internal Cohort Analyses

Person-years at risk and deaths or cancer cases were stratified by variables of interest to input into Epicure. Person-years were stratified by attained age (>15-35, >35-45, >45-55, >55-65, > 65 years), calendar period (1954-1975, 1976-1995, 1996+) and cumulative dose (0, >0-1, >1-5, >5-10, >10-20, >20-30, >30-50, >50-100 and > 100 WLM). The categories for cumulative dose were chosen to have an approximately equal distribution of lung cancer deaths and sufficient numbers to provide reliable risk estimates.

For mortality analyses, person-years were calculated from the latest of January 1, 1954 (start of study period) or date of first employment and ended on the earliest of date of death or December 31, 2007. Similarly for incidence analyses, person-years was calculated from the latest of January 1, 1969 or date of first employment and ended on the earliest of date of death, December 31, 2005 or date of diagnosis for the cancer of interest. Multiple cancer diagnoses were considered for each miner. Where a miner had multiple of the same diagnosis (such as lung cancer), the first lung cancer diagnosis was used in the analysis.

In an effort to minimize the effects of under ascertainment of mortality, analyses were conducted to explore alternate age cutoffs for end of follow-up. Individuals lost to follow up and incorrectly assumed alive at very advanced ages were likely to unduly contribute person years, which would influence results with biased estimates. Thus, after exploration of age cutoffs of 75, 85 , and 100 years of age (results not presented for 75 and 100 years of age) a conservative age cutoff of 85 years of age was chosen in order to limit the effect of loss to follow-up on the results, while not losing too many cases.

Similar to other studies conducted on radon exposure and cancer, Poisson regression modelling for grouped data was used to estimate relative risk estimates. The general equation for Poisson regression modelling is (74, 76):

$$\frac{\lambda}{\lambda_o} = \frac{\exp (b_1X_1 + b_2X_2 + \ldots.. + b_jX_{j)}}{} \quad [1]$$

Where λ represents the mortality/incidence rates for specific values of X_1, X_2, $X_{3\ldots}X_j$

λ_o represents the background or baseline mortality/incidence rate

X_1-X_j represents the independent variables

β_1-β_j represents the regression coefficients to be predicted from the model, which represent the effect of the predictor variable

To examine WLM as a continuous parameter, the linear excess relative risk (ERR) model was used. This model assumes a linear relationship between cumulative radon exposure and risk. The general model for the ERR is (22, 77):

$$RR = 1 + \beta X_1 \quad [2]$$

In this equation β represents the increase in the ERR per unit increase in cumulative exposure (X_1). The AMFIT module in EPICURE was used to conduct all the Poisson regression modeling.

All models were adjusted for calendar period (1954-1975, 1976-1995, 1996 onwards) and attained age (>15-35, >35-45, >45-55, >55-65, > 65 years). Groupings for calendar period and attained age were collapsed for analyses where model convergence could not be reached.

Modification of the exposure-response relationship by other key variables was also assessed. This was evaluated separately for each modifying factor by examining variations in the dose-response (ERR/WLM) relationship within categories of the factor by comparing the baseline model [2] to the following model:

$$RR = 1 + \beta_j X \qquad [3]$$

Where β_j represents the ERR/WLM associated with category *j* (77). This was done for each modifying factor mentioned below. The difference in deviance between the two models was computed as the likelihood ratio statistic. A significant p-value indicated that values of ERR/WLM across categories were not homogeneous. The modifying factors examined included attained age (<55, 55-<60, 60-<65, 65-<75 and 75 + years old), exposure rate (<2, 2-<5, 5-<10, 10+ WLM/yr), time since first exposure (<15, 15-<25, 25-<30, 30-<35, 35-<40, 40-<45, >45 years), time since last exposure (<15, 15-<25, 25-<30, 30-<40, ≥ 40 years) and age at first exposure (<25, ≥ 25-30, ≥ 30-35, ≥35 years old). Similar to cumulative dose, categories for each of the modifying factors were chosen to have an equal distribution of lung cancer deaths and sufficient numbers to provide reliable risk estimates.

The effect on the risk estimate of lagging the cumulative exposure was also examined using lags of 5, 10, 15, and 20 years. To determine the most suitable lag period, Rothman's principle was used, which states that the lag period yielding the highest risk estimates should be used to reduce

non-differential misclassification (78). Based on this principle, as well as a review of previous studies, a lag interval of five years was used in the calculation of cumulative exposure for all lung cancer analyses. Similarly, using Rothman's principles a lag of 2 years was used for stomach cancer and 10 years for both leukemia and cardiovascular diseases in the exploratory analyses of these additional sites with radon exposure.

4.1.3 Lung Cancer Morphology

Our cohort provided enough power to examine the lung cancer cases by morphology. Using the ICD-O codes provided, lung cancers were classified according to the International Agency for Research on Cancer (IARC) histological groupings (79). This included the following four major groupings: squamous cell, adenocarcinoma, small cell and large cell carcinoma. New cumulative dose categories that allowed for an approximately equal distribution of lung cancer deaths within the four major histological groupings were chosen. The exposure categories were >1, 1-10, >10-20, >20-60 and >60 WLM. Standard Poisson regression models were fit to each of the four major groupings as well as all lung cancer deaths with the same cumulative dose categories for comparison.

4.1.4 Modern Miners

Another goal of this study was to evaluate the risk of lung cancer mortality among miners who started employment after 1970 when, as described above, new ventilation practices were introduced in Ontario uranium mines. Poisson regression models were fit to examine these modern miners. Cumulative exposure categories were similar as those originally chosen for the entire cohort to enable comparison with the entire cohort up to the highest cumulative dose category possible. The exposure categories used were 0, >0-1, >1-5 and >5 WLM.

Figure 5: Cohort Inclusion and Exclusion Criteria

National Dose Registry

Mining Master File	Yes	No	Total
Yes	25,271	1,049	26,320
No	4,594	0	4,594
Total	29,865	1,049	**30,914**

(n=103) → Exclude all definite and some possible duplicates (96 definite; 7 possible)

(n=653) → Exclude workers with missing date of birth

(n=476) → Exclude NDR "Spanner Records"

(n=42) → Exclude invalid ages (≤ 15 yrs at first employment or those 65yrs + at entry into study)

(n=66) → Exclude those with start dates after December 31, 1996

(n=600) → Exclude those without at least one uranium mining record (in the NDR)

(n=15) → Validation issues with dates (14 for death prior to end of employment (end date could not be determined) and one with death before cancer)

(n=413) → Exclude women for internal analyses

Women to be included in external analyses only because of small numbers

Final Analysis File
N= 28, 546

5. RESULTS

There were a total of 30,914 uranium miners identified from the NDR and MMF. After further exclusions were applied there were 28,546 male and 413 female miners for use in our analyses. Due to the small number of female miners, they were not included in the internal analyses, but were included in the external analyses. The mean age at entry into the study was 28.8 years for male miners and 27.9 years for female workers. Male miners in the cohort had a mean cumulative exposure of 21.0 WLM, while female workers had a mean cumulative exposure of 0.2 WLM over an average of 5.3 years and 5.9 years of total employment, respectively (Table 3). Most workers were only employed in the Elliot Lake region (n=25,414), with some employed only in Bancroft (n=2,454) and a small portion employed in both the Elliot Lake and Bancroft regions throughout their work history (n=1,030). The other category represents workers who were employed for research, medical or regulatory purposes, with no mention of mine where employment took place or those for which employer could not be determined. The highest mean radon dose was observed among miners who were employed in both the Bancroft and Elliot Lake regions (mean RDP dose=44.5 WLM, SD=51.1), compared to the workers who were employed in only one region. Between 1954 and 2007, a total of 8,572 deaths were observed, and of these 2,809 were due to cancer, including 1,246 lung cancer deaths. There were 4,151 incident cancers, including 1,285 lung cancers, observed. With an age cutoff of 85 years applied a total of 8,318 deaths, including 2,734 malignant cancer deaths (1,230 due to lung cancer) were observed. There were 3,976 incident malignant cancers (excluding non-melanoma skin cancers) including 1,274 first primary or 1,291 multiple primary lung cancers.

Table 3: Basic characteristics of cohort members

Characteristics	Values	Males	Females
Number of subjects	Total	28,546	413
Age at entry into study in years	Median	27.0	25.0
	Mean	28.8	27.9
	Range	16 to 65	17 to 61
Total duration of employment in years	Median	3	5.0
	Mean	5.3	5.9
	Range	1 to 45	1 to 28
Cumulative RDP dose in WLM	Median	5.8	0.0
	Mean	21.0	0.2
	Range	0.0 to 875.1	0.0 to 16.3
Birth Year	**Time Period**	**N (%)**	**N (%)**
	<1900	26 (0.1)	0 (0.0)
	1900-1909	420 (1.5)	0 (0.0)
	1910-1919	1,882 (6.6)	0 (0.0)
	1920-1929	5,211 (18.3)	8 (1.9)
	1930-1939	7,820 (27.4)	31 (7.5)
	1940-1949	4,818 (16.9)	70 (16.9)
	1950-1959	6,621 (23.2)	186 (45.0)
	1960-1969	1,713 (6.0)	115 (27.8)
	>1970	35 (0.1)	3(0.7)
Year first employed	1942-1949	26 (0.1)	0 (0.0)
	1950-1959	12,710 (44.5)	0 (0.0)
	1960-1969	2,533 (8.9)	2 (0.5)
	1970-1979	8,653 (30.3)	56 (13.6)
	1980-1989	4,527 (15.9)	343 (83.1)
	>1990	97	12 (2.9)

Table 4: Exposure characteristics of cohort members by sex and mining region

Characteristic	SUB-COHORT				Total
	Elliot Lake region	Bancroft region	Mixed region	Other	
Number of Subjects	25,414	2,454	1,030	61	28,959
Males (%)	25,014 (98.4)	2,450 (99.8)	1,030 (100.0)	52 (85.2)	28,546 (98.6)
Females (%)	400 (1.6)	4 (0.2)	0 (0.0)	9 (14.8)	413 (1.4)
Mean RDP Dose WLM (SD)					
Males	18.27 (37.1)	39.89 (61.2)	44.52 (51.1)	0.16 (0.4)	21.04 (41.0)
Females	0.22 (1.3)	0.10 (0.1)	0 (0.0)	0.16 (0.4)	0.22 (1.3)
Mean Years Employed (SD)					
Males	5.46 (5.9)	2.95 (2.7)	5.70 (4.9)	6.33 (8.0)	5.25 (5.7)
Females	5.92 (4.6)	2.00 (0.0)	0 (0.0)	6.33 (7.0)	5.89 (4.6)

Figure 6 shows the mean annual radon exposure and the number of miners employed in the cohort from 1954-1996. There was a significant drop in radon exposures in the late 1960's which coincided with the introduction of new ventilation practices in Ontario mines and confirms that the appropriate definition of modern miners would be miners who started employment after 1970.

Figure 6: Mean annual radon exposure and employment 1954-1996

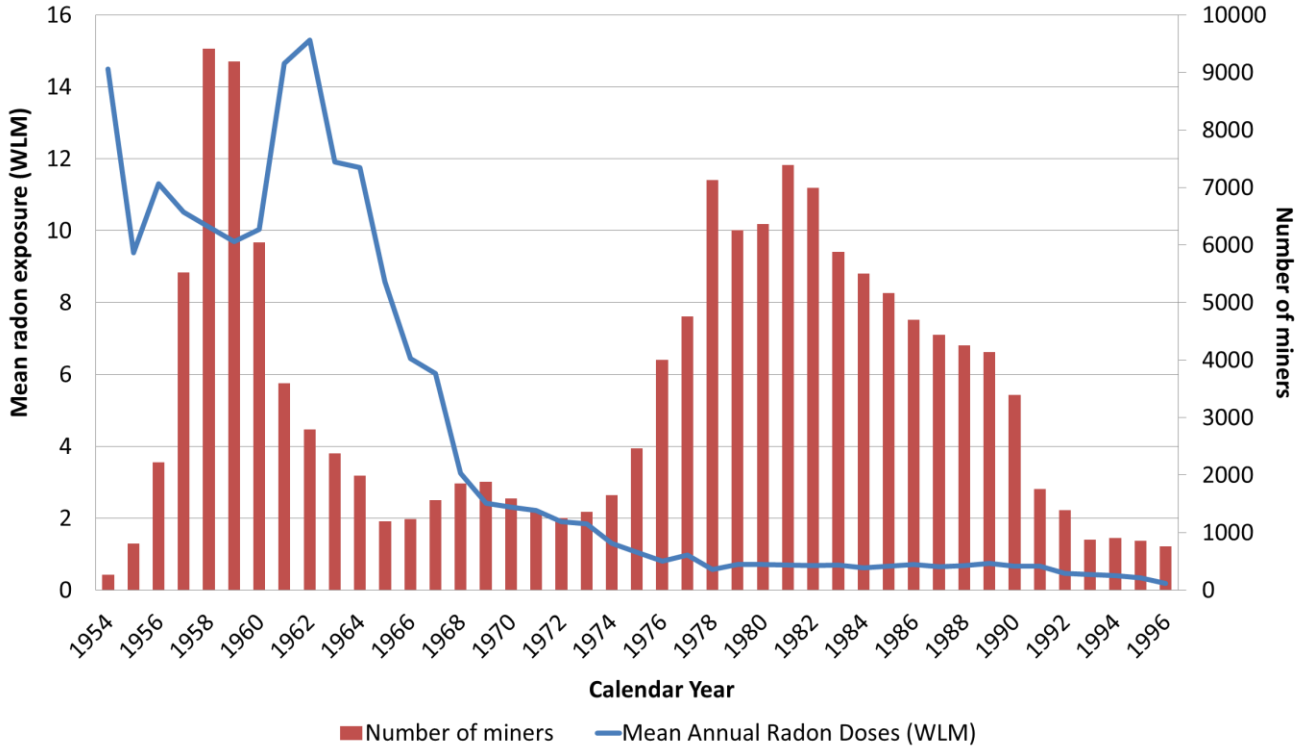
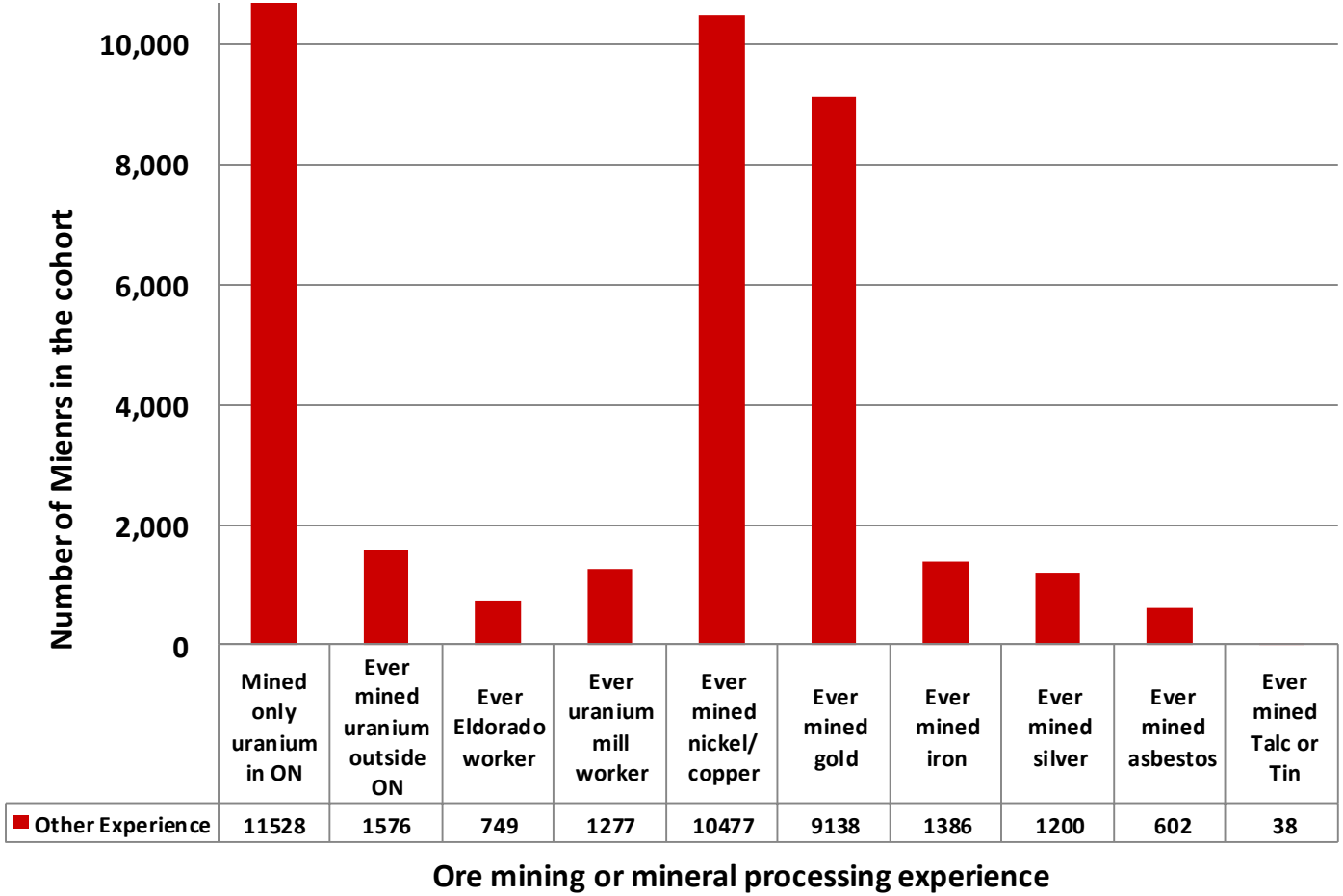


Figure 7 following displays the number of uranium cohort members with experience mining other ores, and also with experience refining uranium or mining it outside of Ontario.

Figure 7: Ontario Uranium Miner Cohort Other Ore Mining Experience



Note: a) Ore mining experience was only available from the MMF records exclusively
b) Uranium mining experience outside of Ontario was available from combined MMF and NDR records

5.1 External comparisons of mortality and cancer incidence

Table 5: Mortality for various non-cancer causes of death and 95% CIs, male, Ontario uranium miners (1954–2007)

ICD-9	CAUSES OF DEATH	OBS	EXP	SMR	95% CI
001-999	All Causes	8318	8762.88	0.95	0.93-0.97
001-139	Infective & Parasitic Diseases	62	116.89	0.53	0.41-0.68
140-239	Neoplasms	2765	2790.44	0.99	0.95-1.03
240-279	Endocrine/Nutritional/ Metabolic Diseases	173	262.36	0.66	0.56-0.77
280-289	Blood Diseases	16	21.72	0.74	0.42-1.20
290-319	Mental Disorders	107	123.38	0.87	0.71-1.05
320-389	Nervous System/Sense Organ Diseases	95	195.21	0.49	0.39-0.59
390-459	Circulatory Disease	2697	3159.16	0.85	0.82-0.89
390-448	Major Cardio-Vascular Diseases	2681	3137.59	0.85	0.82-0.89
410-414, 429.2	Ischemic Heart Disease	1834	2024.41	0.91	0.86-0.95
430-438	Cerebrovascular Disease	315	416.41	0.76	0.68-0.84
460-519	Respiratory Disease	600	588.03	1.02	0.94-1.11
490-492, 496	Chronic Obstructive Pulmonary Disease	333	322.05	1.03	0.93-1.15
011.4, 495, 500-505	Pneumoconiosis	51	5.68	8.98	6.69-11.81
500, 502	Silicosis & Anthracosilicosis	47	2.39	19.68	14.46-26.18
501	Asbestosis	0	2.24		
495, 503-505	Other Pneumoconiosis	4	0.79	5.05	1.36-12.94
011.4	Silicotuberculosis	0	0.26		
520-579	Digestive Disease	323	379.84	0.85	0.76-0.95
580-629	Genitourinary Disease	87	112.21	0.78	0.62-0.96
680-709	Skin/Subcutaneous Tissue Disease	6	5.37	1.12	0.41-2.43
710-739	Musculoskeletal Disease	30	23.03	1.30	0.88-1.86
780-799	Symptoms/Ill-Defined	105	96.22	1.09	0.89-1.32
571	Cirrhosis of Liver	177	193.80	0.91	0.78-1.06
800-999	Accidents/Poisonings/Violence	1247	872.09	1.43	1.35-1.51
E810-819	Motor Vehicle Traffic Accidents	298	235.84	1.26	1.12-1.42
E890-899, E929.4	Fires	41	23.21	1.77	1.27-2.40
E950-959	Suicide	323	241.41	1.34	1.20-1.49
E960-969	Homicide	37	28.43	1.30	0.92-1.79
E850-869	Accidental Poisoning	60	45.50	1.32	1.01-1.70
E880.0-E888	Falls, Unintentional	99	58.20	1.70	1.38-2.07

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3 are suppressed
Ischemic Heart Disease = Reference rates available only from 1970

Table 6: Cancer mortality, incidence and 95% CIs, male Ontario uranium miners

		CANCER MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	**CANCER**	**OBS**	**EXP**	**SMR**	**95% CI**	**OBS**	**EXP**	**SIR**	**95% CI**
140-208	All Cancers	2734	2753.27	0.99	0.96-1.03	3976	5002.22	0.79	0.77-0.82
140-149	Buccal Cavity & Pharyngeal	53	70.62	0.75	0.56-0.98	141	201.61	0.70	0.59-0.82
150	Esophageal	72	81.67	0.88	0.69-1.11	53	68.44	0.77	0.58-1.01
151	Stomach	108	121.29	0.89	0.73-1.08	127	157.59	0.81	0.67-0.96
153-154, 159.0	Colorectal	276	337.44	0.82	0.72-0.92	485	690.16	0.70	0.64-0.77
157	Pancreatic	112	138.65	0.81	0.67-0.97	105	123.04	0.85	0.70-1.03
160	Nasal & Sinus	0	3.65			x	x	0.52	0.17-1.22
161	Laryngeal	44	39.73	1.11	0.80-1.49	83	98.46	0.84	0.67-1.05
162	Lung	1230	917.64	1.34	1.27-1.42	1291	994.66	1.30	1.23-1.37
162	Pleural	5	5.52	0.91	0.29-2.11	na			
170	Bone	5	6.90	0.72	0.23-1.69	7	9.88	0.71	0.28-1.46
164.1, 171	Connective Tissue	8	12.96	0.62	0.27-1.22	17	29.26	0.58	0.34-0.93
172	Malignant Melanoma of the Skin	21	35.45	0.59	0.37-0.91	41	122.38	0.34	0.24-0.45
173	Non-Melanoma Skin Cancer	8	8.33	0.96	0.41-1.89	na			
175	Breast	x	x	0.60	0.07-2.16	12	9.90	1.21	0.63-2.12
185	Prostate	150	209.07	0.72	0.61-0.84	615	1104.19	0.56	0.51-0.60
186	Testis	3	5.93	0.51	0.10-1.48	18	34.83	0.52	0.31-0.82
189.0, 189.2	Kidney	53	71.36	0.74	0.56-0.97	100	159.20	0.63	0.51-0.76
188, 189.3-189.4, 189.8-189.9	Bladder & Other Urinary	66	71.05	0.93	0.72-1.18	196	289.85	0.68	0.58-0.78
191-192	Brain & Other Nervous System	67	83.75	0.80	0.62-1.02	70	90.24	0.78	0.60-0.98
193	Thyroid	6	4.77	1.26	0.46-2.74	17	28.83	0.59	0.340.94
201	Hodgkin's Disease	11	13.74	0.80	0.40-1.43	19	29.95	0.63	0.38-0.99
200, 202	Non-Hodgkin's Lymphoma	97	100.00	0.97	0.79-1.18	163	193.13	0.84	0.72-0.98
203	Multiple Myeloma	25	46.57	0.54	0.35-0.79	49	63.75	0.77	0.57-1.02
204-208	Leukemia	77	94.97	0.81	0.64-1.01	112	138.30	0.81	0.67-0.97

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed na = not available

With a person year cutoff of 85 years of age prior to death, the total deaths identified among Ontario male uranium miners was 8,318 (SMR=0.95, 95% CI: 0.93-0.97) from 1954 to 2007. This was an increase of 6,664 deaths beyond those observed with a follow-up of 1955 to 1981 in the most recent Muller et al. (59) study. Consistent with previous analyses, significant lung cancer elevations were observed for mortality with 1,230 (SMR=1.34, 95% CI: 1.27-1.42) and incidence with 1,291 (SIR=1.30, 95% CI: 1.23-1.37) lung cancers. This can be compared to the most recent Muller et al. (59) and Kusiak et al. (14) lung cancer mortality outcomes (refer to Table 2). Other notable significant elevations observed in the overall male cohort include silicosis (SMR=19.68, 95% CI: 14.46-26.18), and accidents, poisoning and violence deaths (SMR=1.43, 95% CI: 1.35-1.51). All accidental death sub-causes were significantly elevated compared to the Canadian population (refer to Table 5).

All cancer mortality was not significantly different from the Canadian population but all cancer incidence displayed a significant deficit (SIR=0.79, 95% CI: 0.77-0.82). Only lung cancer incidence was observed to be significantly in excess for the overall male cohort. Other typical cancers noted in the uranium miner cohort literature including stomach cancer mortality (SMR=0.89, 95% CI: 0.73-1.08) and incidence (SIR=0.77, 95% CI: 0.67-0.96), were either not significantly different from the general population or displayed a significant deficit respectively. Observed leukemia mortality (SMR=0.81, 95% CI: 0.64-1.01) did not differ from the Canadian population and incidence (SIR=0.81, 95% CI: 0.67-0.97), was borderline significantly reduced (refer to Table 6).

Table 7: Overall mortality, incidence and 95% CIs, female Ontario uranium miners

		MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	**CAUSE**	**OBS**	**EXP**	**SMR**	**95% CI**	**OBS**	**EXP**	**SIR**	**95% CI**
001-999	All Causes of Death	18	21.09	0.85	0.51-1.35	na			
390-459	Circulatory Disease	6	4.00	1.50	0.55-3.27	na			
140-208	All Cancers	7	9.62	0.73	0.29-1.50	19	25.43	0.75	0.45-1.17
157	Pancreatic	<3	x	2.54	0.06-14.14	<6	x	2.86	0.07-15.95
162	Lung	<3	x	0.90	0.11-3.25	<6	x	1.20	0.24-3.52
173	Non-Melanoma Skin Cancer	0				<6	x	0.93	0.02-5.17
175	Breast	<3	x	0.46	0.01-2.55	<6	8.99	0.67	0.24-1.45
185	Cervical & Uterine	0				<6	x	0.80	0.02-4.46
189.0, 189.2	Kidney	0				<6	x	2.04	0.05-11.37
204-208	Leukemia	<3	x	3.63	0.09-20.24	<6	x	4.17	0.50-15.05

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed

Among the 413 women in the Ontario uranium cohort, there were 18 deaths from all causes (SMR=0.85, 95% CI: 0.51-1.35) and only seven from all cancers (SMR=0.73, 95% CI: 0.29-1.50), with 19 incident cancers (0.75, 95% CI: 0.45-1.17). Lung cancer mortality (SMR=0.90, 95% CI: 0.11-3.25) did not differ from the general population but incidence displayed a non-significant elevation (SIR=1.20, 95% CI: 0.24-3.52), while leukemia had observed non-significant elevations for mortality (SMR=3.63, 95% CI: 0.09-20.24) and incidence (SIR=4.17, 95% CI: 0.50-15.05; refer to Table 7). Observed death and incident cancer counts were too small to provide stable estimates and most had to be suppressed due to confidentiality.

Table 8: Mortality for various non-cancer causes of death and 95% CIs, male Ontario uranium miners with gold mining experience (1954–2007)

ICD-9	CAUSES OF DEATH	OBS	EXP	SMR	95% CI
001-999	All Causes	3954	4091.67	0.97	0.94-1.00
001-139	Infective & Parasitic Diseases	23	43.31	0.53	0.34-0.80
140-239	Neoplasms	1283	1285.41	1.00	0.94-1.05
240-279	Endocrine/Nutritional/ Metabolic Diseases	81	118.52	0.68	0.54-0.85
280-289	Blood Diseases	10	10.30	0.97	0.46-1.79
290-319	Mental Disorders	57	56.24	1.01	0.77-1.31
320-389	Nervous System/Sense Organ Diseases	47	89.84	0.52	0.38-0.70
390-459	Circulatory Disease	1338	1579.47	0.85	0.80-0.89
390-448	Major Cardio-Vascular Diseases	1326	1568.69	0.85	0.80-0.89
410-414, 429.2	Ischemic Heart Disease	910	991.17	0.92	0.86-0.98
430-438	Cerebrovascular Disease	140	212.23	0.66	0.55-0.78
460-519	Respiratory Disease	342	298.95	1.14	1.03-1.27
490-492, 496	Chronic Obstructive Pulmonary Disease	186	166.06	1.12	0.96-1.29
011.4, 495, 500-505	Pneumoconiosis	40	2.89	13.82	9.87-18.82
500, 502	Silicosis & Anthracosilicosis	36	1.28	28.10	19.68-38.91
501	Asbestosis	0	1.05		
495, 503-505	Other Pneumoconiosis	4	0.40	9.88	2.66-25.29
011.4	Silicotuberculosis	0	0.16		
520-579	Digestive Disease	166	174.48	0.95	0.81-1.11
580-629	Genitourinary Disease	46	55.57	0.83	0.61-1.10
680-709	Skin/Subcutaneous Tissue Disease	4	2.55	1.57	0.42-4.01
710-739	Musculoskeletal Disease	13	10.68	1.22	0.65-2.08
780-799	Symptoms/Ill-Defined	46	38.48	1.20	0.88-1.59
571	Cirrhosis of Liver	89	85.31	1.04	0.84-1.28
800-999	Accidents/Poisonings/Violence	495	321.43	1.54	1.41-1.68
E810-819	Motor Vehicle Traffic Accidents	105	86.14	1.22	1.00-1.48
E890-899, E929.4	Fires	18	9.35	1.93	1.14-3.04
E950-959	Suicide	114	81.02	1.41	1.16-1.69
E960-969	Homicide	9	9.37	0.96	0.44-1.82
E850-869	Accidental Poisoning	26	14.64	1.78	1.16-2.60
E880.0-E888	Falls, Unintentional	61	27.56	2.21	1.69-2.84

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3 are suppressed
Ischemic Heart Disease = Reference rates available only from 1970

Table 9: Cancer mortality, incidence and 95% CIs, male Ontario uranium miners with gold mining experience

		CANCER MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	**CANCER**	**OBS**	**EXP**	**SMR**	**95% CI**	**OBS**	**EXP**	**SIR**	**95% CI**
140-208	All Cancers	1276	1268.64	1.01	0.95-1.06	1771	2228.57	0.79	0.76-0.83
140-149	Buccal Cavity & Pharyngeal	24	31.33	0.77	0.49-1.14	57	87.68	0.65	0.49-0.84
150	Esophageal	28	35.96	0.78	0.52-1.13	22	30.64	0.72	0.45-1.09
151	Stomach	53	59.11	0.90	0.67-1.17	62	74.00	0.84	0.64-1.07
153-154, 159.0	Colorectal	137	156.70	0.87	0.73-1.03	221	312.05	0.71	0.62-0.81
157	Pancreatic	50	63.89	0.78	0.58-1.03	46	56.65	0.81	0.59-1.08
160	Nasal & Sinus	0	1.64			<6	x	0.49	0.06-1.75
161	Laryngeal	29	18.31	1.58	1.06-2.28	44	44.38	0.99	0.72-1.33
162	Lung	606	425.39	1.42	1.31-1.54	651	461.65	1.41	1.30-1.52
162	Pleural	<3	x	0.79	0.10-2.87	na			
170	Bone	<3	x	0.33	0.01-1.86	<6	x	0.53	0.06-1.92
164.1, 171	Connective Tissue	<3	x	0.19	0.00-1.06	9	11.69	0.77	0.35-1.46
172	Malignant Melanoma of the Skin	9	14.19	0.63	0.29-1.20	13	45.78	0.28	0.15-0.49
173	Non-Melanoma Skin Cancer	4	3.85	1.04	0.28-2.66	na			
175	Breast	<3	x	0.65	0.02-3.60	3	4.39	0.68	0.14-2.00
185	Prostate	65	106.11	0.61	0.47-0.78	254	502.00	0.51	0.45-0.57
186	Testis	0	2.25			<6	x	0.36	0.07-1.05
189.0, 189.2	Kidney	19	31.93	0.60	0.36-0.93	33	67.21	0.49	0.34-0.69
188, 189.3-189.4, 189.8-189.9	Bladder & Other Urinary	21	34.47	0.61	0.38-0.93	77	135.20	0.57	0.45-0.71
191-192	Brain & Other Nervous System	24	34.96	0.69	0.44-1.02	30	35.84	0.84	0.56-1.19
193	Thyroid	<3	x	0.94	0.11-3.38	<6	x	0.41	0.11-1.05
201	Hodgkin's Disease	3	5.99	0.50	0.10-1.46	10	9.82	1.02	0.49-1.87
200, 202	Non-Hodgkin's Lymphoma	36	43.61	0.83	0.58-1.14	62	78.33	0.79	0.61-1.01
203	Multiple Myeloma	9	21.49	0.42	0.19-0.79	22	28.79	0.76	0.48-1.16
204-208	Leukemia	39	42.89	0.91	0.65-1.24	46	60.21	0.76	0.56-1.02

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed na = not available

Table 10: Mortality for various non-cancer causes of death and 95% CIs, male Ontario uranium miners without gold mining experience (1954–2007)

ICD-9	CAUSES OF DEATH	OBS	EXP	SMR	95% CI
001-999	All Causes	3956	4320.49	0.92	0.89-0.94
001-139	Infective & Parasitic Diseases	34	64.99	0.52	0.36-0.73
140-239	Neoplasms	1351	1391.64	0.97	0.92-1.02
240-279	Endocrine/Nutritional/ Metabolic Diseases	79	132.56	0.60	0.47-0.74
280-289	Blood Diseases	5	10.56	0.47	0.15-1.11
290-319	Mental Disorders	44	61.96	0.71	0.52-0.95
320-389	Nervous System/Sense Organ Diseases	42	97.33	0.43	0.31-0.58
390-459	Circulatory Disease	1239	1475.03	0.84	0.79-0.89
390-448	Major Cardio-Vascular Diseases	1235	1464.94	0.84	0.80-0.89
410-414, 429.2	Ischemic Heart Disease	833	962.35	0.87	0.81-0.93
430-438	Cerebrovascular Disease	162	191.08	0.85	0.72-0.99
460-519	Respiratory Disease	238	270.72	0.88	0.77-1.00
490-492, 496	Chronic Obstructive Pulmonary Disease	136	146.49	0.93	0.78-1.10
011.4, 495, 500-505	Pneumoconiosis	11	2.61	4.21	2.10-7.54
500, 502	Silicosis & Anthracosilicosis	11	1.04	10.58	5.27-18.92
501	Asbestosis	0	1.11		
495, 503-505	Other Pneumoconiosis	0	0.36		
011.4	Silicotuberculosis	0	0.10		
520-579	Digestive Disease	141	190.14	0.74	0.62-0.87
580-629	Genitourinary Disease	36	53.02	0.68	0.48-0.94
680-709	Skin/Subcutaneous Tissue Disease	<3	x	0.38	0.01-2.14
710-739	Musculoskeletal Disease	16	11.43	1.40	0.80-2.27
780-799	Symptoms/Ill-Defined	53	51.63	1.03	0.77-1.34
571	Cirrhosis of Liver	80	100.10	0.80	0.63-0.99
800-999	Accidents/Poisonings/Violence	675	497.41	1.36	1.26-1.46
E810-819	Motor Vehicle Traffic Accidents	171	136.70	1.25	1.07-1.45
E890-899, E929.4	Fires	23	12.70	1.81	1.15-2.72
E950-959	Suicide	182	141.71	1.28	1.10-1.49
E960-969	Homicide	25	16.94	1.48	0.95-2.18
E850-869	Accidental Poisoning	31	26.98	1.15	0.78-1.63
E880.0-E888	Falls, Unintentional	33	28.55	1.16	0.80-1.62

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3 are suppressed
Ischemic Heart Disease = Reference rates available only from 1970

Table 11: Cancer mortality, incidence and 95% CIs, male Ontario uranium miners without gold mining experience

		CANCER MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	CANCER	OBS	EXP	SMR	95% CI	OBS	EXP	SIR	95% CI
140-208	All Cancers	1330	1372.82	0.97	0.92-1.02	1964	2548.97	0.77	0.74-0.81
140-149	Buccal Cavity & Pharyngeal	26	36.14	0.72	0.47-1.05	74	104.42	0.71	0.56-0.89
150	Esophageal	40	41.97	0.95	0.68-1.30	28	34.80	0.80	0.53-1.16
151	Stomach	50	57.84	0.86	0.64-1.14	58	77.38	0.75	0.57-0.97
153-154, 159.0	Colorectal	124	167.26	0.74	0.62-0.88	231	348.46	0.66	0.58-0.75
157	Pancreatic	55	69.07	0.80	0.60-1.04	52	61.32	0.85	0.63-1.11
160	Nasal & Sinus	0	1.85			<6	x	0.60	0.12-1.77
161	Laryngeal	14	19.85	0.71	0.39-1.18	34	49.99	0.68	0.47-0.95
162	Lung	570	456.06	1.25	1.15-1.36	581	493.92	1.18	1.08-1.28
162	Pleural	<3	x	0.72	0.09-2.60	na			
170	Bone	4	3.58	1.12	0.30-2.86	<6	x	0.91	0.29-2.13
164.1, 171	Connective Tissue	7	6.96	1.01	0.40-2.07	8	15.85	0.50	0.22-0.99
172	Malignant Melanoma of the Skin	9	19.29	0.47	0.21-0.89	25	68.62	0.36	0.24-0.54
173	Non-Melanoma Skin Cancer	4	4.13	0.97	0.26-2.48	na			
175	Breast	<3	x	0.60	0.02-3.35	7	5.07	1.38	0.55-2.84
185	Prostate	81	96.49	0.84	0.67-1.04	315	556.24	0.57	0.51-0.63
186	Testis	3	3.39	0.88	0.18-2.58	14	22.40	0.63	0.34-1.05
189.0, 189.2	Kidney	33	36.28	0.91	0.63-1.28	63	83.88	0.75	0.58-0.96
188, 189.3-189.4, 189.8-189.9	Bladder & Other Urinary	40	34.05	1.17	0.84-1.60	104	143.17	0.73	0.59-0.88
191-192	Brain & Other Nervous System	40	44.46	0.90	0.64-1.23	38	49.11	0.77	0.55-1.06
193	Thyroid	4	2.42	1.65	0.44-4.23	9	16.76	0.54	0.24-1.02
201	Hodgkin's Disease	7	7.24	0.97	0.39-1.99	7	17.72	0.39	0.16-0.81
200, 202	Non-Hodgkin's Lymphoma	56	51.73	1.08	0.82-1.41	88	103.78	0.85	0.68-1.04
203	Multiple Myeloma	15	23.20	0.65	0.36-1.07	24	32.18	0.75	0.48-1.11
204-208	Leukemia	35	48.08	0.73	0.51-1.01	59	71.37	0.83	0.63-1.07

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio

95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed na = not available

Analyses concerning uranium miners with and without gold mining experience were conducted which showed that there were 3,954 (43%) deaths among 9,138 miners with gold mining experience. Non-cancer respiratory diseases were significantly elevated among this group (SMR=1.12, 95% CI: 1.03-1.27), and in particular the sub-category of silicosis deaths (SMR=28.10, 95% CI: 19.68-38.91), which account for 77% of silicosis deaths in the overall cohort. Otherwise, significant elevations were observed throughout accidents, poisoning and violence sub-categories (SMR=1.54, 95% CI: 1.41-1.68; refer to Table 8). Lung cancer mortality (SMR=1.42, 95% CI: 1.31-1.54) and incidence (SIR=1.41, 95% CI: 1.30-1.52) were also significantly elevated in the ever gold miner group. Of particular interest is the observed laryngeal cancer mortality elevation in the ever gold group (SMR=1.58, 95% CI: 1.06-2.28; refer to Table 9).

For the 16,503 uranium miners without gold mining experience there were 3,956 (24%) all cause deaths. Silicosis deaths were significantly elevated for this group (SMR=10.58, 95% CI: 5.27-18.92) but comprised only 23% of silicosis deaths in the cohort. Accidents, poisoning, and violent deaths (SMR=1.43, 95% CI: 1.35-1.51) along with most sub-causes of death were also significantly elevated for the never gold mining group (refer to Table 10). Lung cancer mortality (SMR=1.25, 95% CI: 1.15-1.36) and incidence (SIR=1.18, 95% CI: 1.08-1.28) were also observed to be significantly elevated for the uranium never gold miners group (refer to Table 11).

Table 12: Mortality for various non-cancer causes of death and 95% CIs, male Ontario uranium miners with only Elliot Lake experience (1954–2007)

ICD-9	CAUSES OF DEATH	OBS	EXP	SMR	95% CI
001-999	All Causes	6834	7213.02	0.95	0.93-0.97
001-139	Infective & Parasitic Diseases	50	100.37	0.50	0.37-0.66
140-239	Neoplasms	2280	2302.80	0.99	0.95-1.03
240-279	Endocrine/Nutritional/ Metabolic Diseases	135	217.38	0.62	0.52-0.74
280-289	Blood Diseases	11	17.83	0.62	0.31-1.10
290-319	Mental Disorders	83	102.29	0.81	0.65-1.01
320-389	Nervous System/Sense Organ Diseases	79	161.41	0.49	0.39-0.61
390-459	Circulatory Disease	2196	2566.26	0.86	0.82-0.89
390-448	Major Cardio-Vascular Diseases	2183	2548.75	0.86	0.82-0.89
410-414, 429.2	Ischemic Heart Disease	1493	1653.12	0.90	0.86-0.95
430-438	Cerebrovascular Disease	257	336.79	0.76	0.67-0.86
460-519	Respiratory Disease	463	476.51	0.97	0.89-1.06
490-492, 496	Chronic Obstructive Pulmonary Disease	249	260.40	0.96	0.84-1.08
011.4, 495, 500-505	Pneumoconiosis	46	4.59	10.03	7.34-13.37
500, 502	Silicosis & Anthracosilicosis	44	1.91	23.07	16.76-30.97
501	Asbestosis	0	1.84		
495, 503-505	Other Pneumoconiosis	<3	x	3.12	0.38-11.28
011.4	Silicotuberculosis	0	0.20		
520-579	Digestive Disease	265	313.60	0.85	0.75-0.95
580-629	Genitourinary Disease	76	91.25	0.83	0.66-1.04
680-709	Skin/Subcutaneous Tissue Disease	6	4.40	1.36	0.50-2.97
710-739	Musculoskeletal Disease	28	19.00	1.47	0.98-2.13
780-799	Symptoms/Ill-Defined	89	81.59	1.09	0.88-1.34
571	Cirrhosis of Liver	137	161.24	0.85	0.71-1.00
800-999	Accidents/Poisonings/Violence	1068	743.97	1.44	1.35-1.52
E810-819	Motor Vehicle Traffic Accidents	255	200.42	1.27	1.12-1.44
E890-899, E929.4	Fires	32	19.56	1.64	1.12-2.31
E950-959	Suicide	286	209.72	1.36	1.21-1.53
E960-969	Homicide	34	24.70	1.38	0.95-1.92
E850-869	Accidental Poisoning	46	39.75	1.16	0.85-1.54
E880.0-E888	Falls, Unintentional	80	47.67	1.68	1.33-2.09

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3 are suppressed
Ischemic Heart Disease = Reference rates available only from 1970

Table 13: Cancer mortality, incidence and 95% CIs, male with only Elliot Lake region uranium mining experience

		CANCER MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	**CANCER**	**OBS**	**EXP**	**SMR**	**95% CI**	**OBS**	**EXP**	**SIR**	**95% CI**
140-208	All Cancers	2255	2271.97	0.99	0.95-1.03	3335	4155.96	0.80	0.78-0.83
140-149	Buccal Cavity & Pharyngeal	42	58.65	0.72	0.52-0.97	122	168.27	0.73	0.60-0.87
150	Esophageal	61	67.96	0.90	0.69-1.15	47	56.80	0.83	0.61-1.10
151	Stomach	93	98.93	0.94	0.76-1.15	111	129.68	0.86	0.70-1.03
153-154, 159.0	Colorectal	232	278.00	0.83	0.73-0.95	426	571.83	0.74	0.68-0.82
157	Pancreatic	96	114.39	0.84	0.68-1.02	89	101.63	0.88	0.70-1.08
160	Nasal & Sinus	0	3.03			<6	x	0.63	0.20-1.46
161	Laryngeal	38	32.76	1.16	0.82-1.59	69	81.59	0.85	0.66-1.07
162	Lung	1001	756.39	1.32	1.24-1.41	1049	820.25	1.28	1.20-1.36
163	Pleural	4	4.56	0.88	0.24-2.24	Na			
170	Bone	3	5.73	0.52	0.11-1.53	<6	x	0.59	0.19-1.38
164.1, 171	Connective Tissue	5	10.94	0.46	0.15-1.07	11	24.81	0.44	0.22-0.79
172	Malignant Melanoma of the Skin	16	29.99	0.53	0.30-0.87	31	104.80	0.30	0.20-0.42
173	Non-Melanoma Skin Cancer	7	6.87	1.02	0.41-2.10	na			
175	Breast	2	2.77	0.72	0.09-2.61	10	8.24	1.21	0.58-2.23
185	Prostate	120	169.54	0.71	0.59-0.85	512	912.42	0.56	0.51-0.61
186	Testis	<3	x	0.40	0.05-1.44	17	31.56	0.54	0.31-0.86
189.0, 189.2	Kidney	47	59.22	0.79	0.58-1.06	90	133.58	0.67	0.54-0.83
188, 189.3-189.4, 189.8-189.9	Bladder & Other Urinary	54	58.07	0.93	0.70-1.21	162	238.90	0.68	0.58-0.79
191-192	Brain & Other Nervous System	59	70.32	0.84	0.64-1.08	61	76.54	0.80	0.61-1.02
193	Thyroid	6	3.95	1.52	0.55-3.30	17	25.05	0.68	0.40-1.09
201	Hodgkin's Disease	8	11.38	0.70	0.30-1.39	16	26.16	0.61	0.35-0.99
200, 202	Non-Hodgkin's Lymphoma	82	83.35	0.98	0.78-1.22	137	163.23	0.84	0.70-0.99
203	Multiple Myeloma	20	38.42	0.52	0.32-0.80	43	52.85	0.81	0.59-1.10
204-208	Leukemia	65	78.59	0.83	0.64-1.05	99	115.47	0.86	0.70-1.04

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed

Table 14: Mortality for various non-cancer causes of death and 95% CIs, male Ontario uranium miners from the Bancroft region (1954–2007)

ICD-9	CAUSES OF DEATH	OBS	EXP	SMR	95% CI
001-999	All Causes	1004	1122.24	0.89	0.84-0.95
001-139	Infective & Parasitic Diseases	7	11.76	0.60	0.24-1.23
140-239	Neoplasms	325	351.37	0.92	0.83-1.03
240-279	Endocrine/Nutritional/ Metabolic Diseases	27	32.46	0.83	0.55-1.21
280-289	Blood Diseases	4	2.84	1.41	0.38-3.61
290-319	Mental Disorders	17	15.20	1.12	0.65-1.79
320-389	Nervous System/Sense Organ Diseases	12	24.45	0.49	0.25-0.86
390-459	Circulatory Disease	347	433.73	0.80	0.72-0.89
390-448	Major Cardio-Vascular Diseases	344	430.75	0.80	0.72-0.89
410-414, 429.2	Ischemic Heart Disease	232	270.00	0.86	0.75-0.98
430-438	Cerebrovascular Disease	43	58.82	0.73	0.53-0.98
460-519	Respiratory Disease	90	82.09	1.10	0.88-1.35
490-492, 496	Chronic Obstructive Pulmonary Disease	61	45.42	1.34	1.03-1.73
011.4, 495, 500-505	Pneumoconiosis	3	0.80	3.74	0.75-10.93
500, 502	Silicosis & Anthracosilicosis	<3	x	2.78	0.07-15.47
501	Asbestosis	0	0.28		
495, 503-505	Other Pneumoconiosis	<3	x	18.07	2.19-65.28
011.4	Silicotuberculosis	0	0.05		
520-579	Digestive Disease	40	47.54	0.84	0.60-1.15
580-629	Genitourinary Disease	6	15.34	0.39	0.14-0.85
680-709	Skin/Subcutaneous Tissue Disease	0	0.70		
710-739	Musculoskeletal Disease	<3	x	0.34	0.01-1.91
780-799	Symptoms/Ill-Defined	9	10.45	0.86	0.39-1.63
571	Cirrhosis of Liver	26	23.04	1.13	0.74-1.65
800-999	Accidents/Poisonings/Violence	119	89.59	1.33	1.10-1.59
E810-819	Motor Vehicle Traffic Accidents	29	24.69	1.17	0.79-1.69
E890-899, E929.4	Fires	6	2.58	2.33	0.85-5.07
E950-959	Suicide	23	22.05	1.04	0.66-1.57
E960-969	Homicide	0	2.57		
E850-869	Accidental Poisoning	10	3.99	2.51	1.20-4.61
E880.0-E888	Falls, Unintentional	13	7.63	1.70	0.91-2.91

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3 are suppressed
Ischemic Heart Disease = Reference rates available only from 1970

Table 15: Cancer mortality, incidence and 95% CIs, male with only Bancroft region uranium mining experience

		CANCER MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	**CANCER**	**OBS**	**EXP**	**SMR**	**95% CI**	**OBS**	**EXP**	**SIR**	**95% CI**
140-208	All Cancers	319	346.80	0.92	0.82-1.03	430	605.43	0.71	0.64-0.78
140-149	Buccal Cavity & Pharyngeal	7	8.54	0.82	0.33-1.69	12	23.68	0.51	0.26-0.89
150	Esophageal	7	9.82	0.71	0.29-1.47	<6	x	0.48	0.13-1.23
151	Stomach	11	16.29	0.68	0.34-1.21	12	20.12	0.60	0.31-1.04
153-154, 159.0	Colorectal	34	42.94	0.79	0.55-1.11	46	84.79	0.54	0.40-0.72
157	Pancreatic	14	17.49	0.80	0.44-1.34	14	15.38	0.91	0.50-1.53
160	Nasal & Sinus	0	0.45			0	1.11		
161	Laryngeal	3	4.99	0.60	0.12-1.76	10	11.97	0.84	0.40-1.54
162	Lung	143	115.90	1.23	1.04-1.45	144	124.85	1.15	0.97-1.36
163	Pleural	1	0.68	1.46	0.04-8.16	na			
170	Bone	1	0.83	1.20	0.03-6.67	<6	x	0.98	0.02-5.47
164.1, 171	Connective Tissue	<3	x	1.39	0.17-5.03	<6	x	1.59	0.51-3.70
172	Malignant Melanoma of the Skin	3	3.85	0.78	0.16-2.27	6	12.35	0.49	0.18-1.06
173	Non-Melanoma Skin Cancer	<3	x	0.94	0.02-5.26	na			
175	Breast	0	0.42			x	x	1.68	0.20-6.07
185	Prostate	20	29.09	0.69	0.42-1.06	74	137.83	0.54	0.42-0.67
186	Testis	<3	x	1.57	0.04-8.76	<6	x	0.45	0.01-2.49
189.0, 189.2	Kidney	6	8.70	0.69	0.25-1.50	8	18.18	0.44	0.19-0.87
188, 189.3-189.4, 189.8-189.9	Bladder & Other Urinary	9	9.48	0.95	0.43-1.80	22	36.66	0.60	0.38-0.91
191-192	Brain & Other Nervous System	7	9.50	0.74	0.30-1.52	6	9.66	0.62	0.23-1.35
193	Thyroid	0	0.59			0	2.64		
201	Hodgkin's Disease	0	1.67			0	2.64		
200, 202	Non-Hodgkin's Lymphoma	12	11.91	1.01	0.52-1.76	21	21.19	0.99	0.61-1.51
203	Multiple Myeloma	3	5.88	0.51	0.10-1.49	<6	x	0.26	0.03-0.93
204-208	Leukemia	11	11.79	0.93	0.47-1.67	12	16.35	0.73	0.38-1.28

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed na = not available

Table 16: Mortality for various non-cancer causes of death and 95% CIs, male Ontario uranium miners with Mixed Elliot Lake and Bancroft region experience (1954–2007)

ICD-9	CAUSES OF DEATH	OBS	EXP	SMR	95% CI
001-999	All Causes	472	421.60	1.12	1.02-1.23
001-139	Infective & Parasitic Diseases	4	4.61	0.87	0.23-2.22
140-239	Neoplasms	158	134.34	1.18	1.00-1.37
240-279	Endocrine/Nutritional/ Metabolic Diseases	11	12.33	0.89	0.44-1.60
280-289	Blood Diseases	<3	x	0.97	0.02-5.38
290-319	Mental Disorders	6	5.80	1.03	0.38-2.25
320-389	Nervous System/Sense Organ Diseases	3	9.21	0.33	0.07-0.95
390-459	Circulatory Disease	153	157.38	0.97	0.82-1.14
390-448	Major Cardio-Vascular Diseases	153	156.30	0.98	0.83-1.15
410-414, 429.2	Ischemic Heart Disease	108	100.06	1.08	0.89-1.30
430-438	Cerebrovascular Disease	15	20.58	0.73	0.41-1.20
460-519	Respiratory Disease	46	29.12	1.58	1.16-2.11
490-492, 496	Chronic Obstructive Pulmonary Disease	22	16.07	1.37	0.86-2.07
011.4, 495, 500-505	Pneumoconiosis	<3	x	7.06	0.86-25.51
500, 502	Silicosis & Anthracosilicosis	<3	x	16.80	2.04-60.70
501	Asbestosis	0	0.11		
495, 503-505	Other Pneumoconiosis	0	0.04		
011.4	Silicotuberculosis	0	0.01		
520-579	Digestive Disease	18	18.44	0.98	0.58-1.54
580-629	Genitourinary Disease	5	5.56	0.90	0.29-2.10
680-709	Skin/Subcutaneous Tissue Disease	0	0.26		
710-739	Musculoskeletal Disease	<3	x	0.91	0.02-5.07
780-799	Symptoms/Ill-Defined	7	4.07	1.72	0.69-3.54
571	Cirrhosis of Liver	14	9.37	1.49	0.82-2.51
800-999	Accidents/Poisonings/Violence	59	37.58	1.57	1.19-2.03
E810-819	Motor Vehicle Traffic Accidents	13	10.49	1.24	0.66-2.12
E890-899, E929.4	Fires	3	1.05	2.85	0.57-8.34
E950-959	Suicide	14	9.31	1.50	0.82-2.52
E960-969	Homicide	3	1.11	2.69	0.54-7.86
E850-869	Accidental Poisoning	4	1.70	2.36	0.63-6.03
E880.0-E888	Falls, Unintentional	6	2.86	2.10	0.77-4.56

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3 are suppressed
Ischemic Heart Disease = Reference rates available only from 1970

Table 17: Cancer mortality, incidence and 95% CIs, male with mixed Elliot Lake and Bancroft mining experience

		CANCER MORTALITY 1954-2007				CANCER INCIDENCE 1969-2005			
ICD-9	**CANCER**	**OBS**	**EXP**	**SMR**	**95% CI**	**OBS**	**EXP**	**SIR**	**95% CI**
140-208	All Cancers	158	132.59	1.19	1.01-1.39	207	236.97	0.87	0.76-1.00
140-149	Buccal Cavity & Pharyngeal	4	3.37	1.19	0.32-3.04	7	9.49	0.74	0.30-1.52
150	Esophageal	4	3.83	1.04	0.28-2.67	<6	x	0.31	0.01-1.70
151	Stomach	4	5.99	0.67	0.18-1.71	<6	x	0.52	0.14-1.33
153-154, 159.0	Colorectal	10	16.28	0.61	0.29-1.13	13	33.03	0.39	0.21-0.67
157	Pancreatic	<3	x	0.30	0.04-1.08	<6	x	0.34	0.04-1.22
160	Nasal & Sinus	0	0.17			0	0.44		
161	Laryngeal	3	1.94	1.54	0.31-4.51	<6	x	0.83	0.222.12
162	Lung	84	44.74	1.88	1.50-2.32	96	48.90	1.96	1.59-2.40
163	Pleural	0	0.27			na			
170	Bone	<3	x	3.09	0.08-17.22	<6	x	2.44	0.06-13.59
164.1, 171	Connective Tissue	<3	x	1.75	0.04-9.76	<6	x	0.79	0.02-4.40
172	Malignant Melanoma of the Skin	<3	x	1.28	0.15-4.61	<6	x	0.79	0.21-2.01
173	Non-Melanoma Skin Cancer	0	0.39			na			
175	Breast	0	0.16			0	0.47		
185	Prostate	9	10.34	0.87	0.40-1.65	28	53.16	0.53	0.35-0.76
186	Testis	0	0.28			0	0.97		
189.0, 189.2	Kidney	0	3.38			<6	x	0.27	0.03-3.82
188, 189.3-189.4, 189.8-189.9	Bladder & Other Urinary	3	3.46	0.87	0.17-2.54	12	14.09	0.85	0.44-1.49
191-192	Brain & Other Nervous System	<3	x	0.26	0.01-1.45	<6	x	0.76	0.15-2.22
193	Thyroid	0	0.22			0	1.10		
201	Hodgkin's Disease	3	0.69	4.36	0.88-12.73	<6	x	2.72	0.55-7.95
200, 202	Non-Hodgkin's Lymphoma	3	4.66	0.64	0.13-1.88	<6	x	0.59	0.19-1.37
203	Multiple Myeloma	<3	x	0.89	0.11-3.22	<6	x	1.32	0.35-3.37
204-208	Leukemia	<3	x	0.22	0.01-1.23	<6	x	0.16	0.00-0.87

Obs = Observed Exp = Expected SMR = Standardized Mortality Ratio SIR = Standardized Incidence Ratio
95% CI = 95% Confidence Interval x = Observed cells under 3for mortality and under 6 for incidence are suppressed na = not available

Regional dichotomies amongst Ontario uranium miners were also analyzed with 6,834 deaths among 25,014 male miners who only worked in Elliot Lake mines, 1,004 deaths among 2,450 miners who only worked in Bancroft area mines, and 472 deaths among 1,030 miners who had worked in both uranium mining regions. It was notable that 94% of silicosis deaths in the cohort occurred among Elliot Lake only miners (SMR=23.07, 95% CI: 16.76-30.97). Once again observed accidents, poisoning, and violence deaths were significantly elevated for this sub-group of miners (SMR=1.44, 95% CI: 1.35-1.52; refer to Table 12). Lung cancer mortality (SMR=1.32, 95% CI: 1.24-1.41) and incidence (SIR=1.28, 95% CI: 1.20-1.36) were also significantly in excess for the Elliot Lake sub-group (refer to Table 13). However, the Bancroft region only mining group did not have a significant excess of silicosis deaths, and only an unstable estimated excess in other pneumoconiosis (SMR=18.07, 95% CI: 2.19-65.28). Accidents, poisoning, and violence deaths (SMR=1.33, 95% CI: 1.10-1.59) for Bancroft miners were significantly in excess, though only the accidental poisoning sub-cause was significantly in excess (SMR=2.51, 95% CI: 1.20-4.61; refer to Table 14). Observed lung cancer mortality (SMR=1.23, 95% CI: 1.04-1.45) was significantly in excess though incidence (SIR=1.15, 95% CI: 0.97-1.36) was borderline and did not reach significant difference with the Canadian population (refer to Table 15).

Those with experience in both of Ontario's major uranium mining regions had significant though unstable estimated elevations in silicosis mortality (SMR=16.80, 95% CI: 2.04-60.70), and significant elevations in overall non-cancer respiratory diseases (SMR=1.58, 95% CI: 1.16-2.11). There were also observed significant elevations in the overall accidents, poisoning, violence category (SMR=1.57, 95% CI: 1.19-2.03) though no other accident death sub-causes (refer to Table 16). All cancer mortality in the mixed region miner group was significantly elevated (SMR=1.19, 95% CI:

1.01-1.39) as were lung cancer mortality (SMR=1.88, 95% CI: 1.50-2.32) and lung cancer incidence (SIR=1.96, 95% CI: 1.59-2.40; refer to Table 17). Otherwise, of interest is the lung cancer mortality and incidence experience of those with NDR only records and no counterpart in the MMF work history data who could not be allocated to other ore mining experience groups. Significant lung cancer mortality (SMR=1.47, 95% CI: 1.10-1.92) and incidence (SIR=1.51, 95% CI: 1.15-1.95) were observed for this group of 2,905 cohort members comprised only of NDR records.

5.2 Internal Analyses

5.2.1 Radon exposure and lung cancer mortality

Tables 18 and 19 demonstrate the risk of lung cancer mortality with increasing cumulative radon exposure for no lag and with a five year lag applied. Several different lag periods (five, 10, 15 and 20) were assessed and, as per Rothman's principle, the five year lag period was chosen because it yielded the highest risk estimates.

Overall, there was a dose-response relationship between cumulative radon exposure and lung cancer mortality (Figure 8). The risk estimates for lung cancer mortality increased with increasing cumulative exposure, although an increased risk was observed at really low doses (>0-1 WLM) (RR=1.43, 95% CI: 1.04-1.95) with a five year lag applied. Workers in the highest cumulative exposure category (>100 WLM) had over a two-fold increase in the risk of lung cancer mortality compared to the unexposed group (RR= 2.32, 95% CI: 1.72-3.14). Using the continuous WLM, the excess relative risk estimate was 0.64/100 WLM (95% CI: 0.42-0.86) with no lag applied and 0.66/100 WLM (95% CI: 0.44-0.87) with a five-year lag, while adjusting for age and calendar period (Figure 8).

Table 18: Lung cancer mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, no lag applied

Cumulative exposure (WLM)	Mean exposure (WLM)[a]	Person-years	Lung cancer deaths	Relative Risk[b]	95% CI
0	0	60770	53	1	*
>0-1	0.36	176657	127	1.29	0.93-1.78
>1-5	2.65	200520	163	1.11	0.81-1.51
>5-10	7.23	131554	121	0.96	0.70-1.33
>10-20	14.3	150828	178	1.11	0.82-1.51
>20-30	24.4	73451	111	1.28	0.92-1.78
>30-50	38.6	80912	146	1.43	1.04-1.96
>50-100	70	71150	164	1.66	1.21-2.25
>100	163.1	52749	167	2.12	1.55-2.89

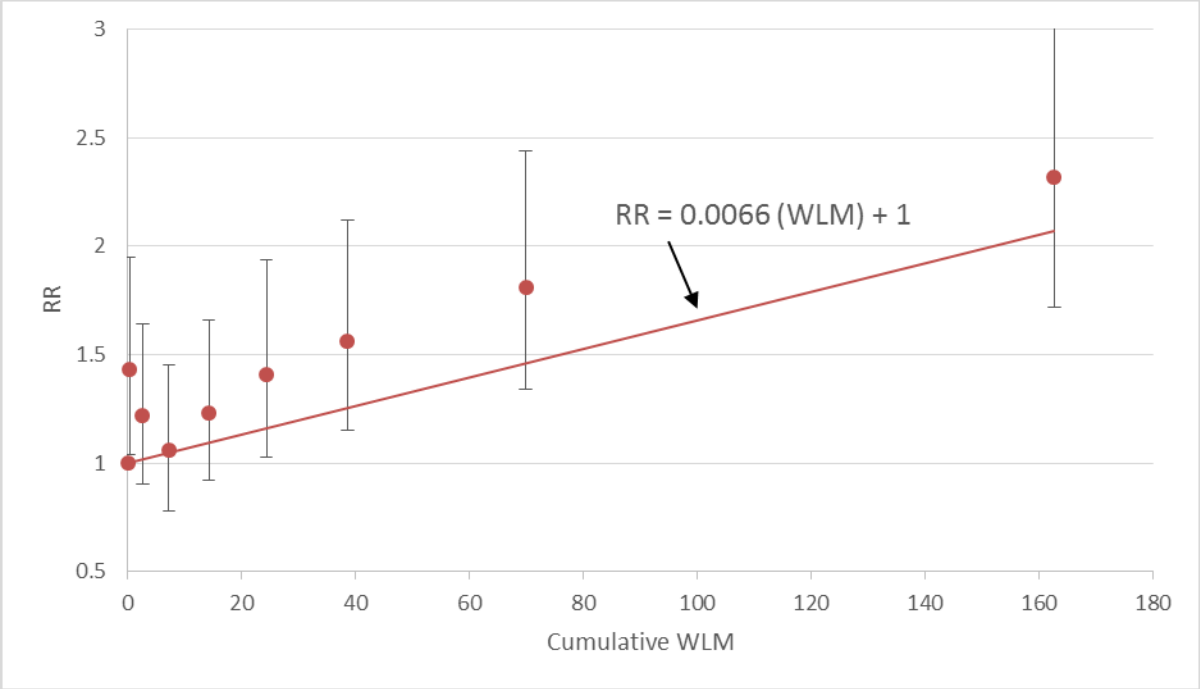
* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Table 19: Lung cancer mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, 5 year lag applied

Cumulative exposure (WLM)	Mean exposure (WLM)[a]	Person-years	Lung cancer deaths	Relative Risk[b]	95% CI
0	0	192941	59	1	*
>0-1	0.37	148015	125	1.43	1.04-1.95
>1-5	2.66	171811	162	1.22	0.90-1.64
>5-10	7.22	113763	121	1.06	0.78-1.45
>10-20	14.3	130136	179	1.23	0.92-1.66
>20-30	24.4	63771	111	1.41	1.03-1.94
>30-50	38.6	70583	145	1.56	1.15-2.12
>50-100	69.9	62087	163	1.81	1.34-2.44
>100	162.7	45484	165	2.32	1.72-3.14

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Figure 8: Relative risk of lung cancer mortality by cumulative exposure to radon and ERR/WLM, with a five year lag applied



Modifying Factors

Results for testing the impact of various modifying factors are presented below for no lag and with a five year lag applied. Several different lag periods (five, 10, 15 and 20) were assessed and, as per Rothman's principle, the five year lag period was chosen because it yielded the highest risk estimates.

5.2.2 Attained Age

The excess relative risk was modified by category of attained age with the risk decreasing with an increase in age at follow-up (Tables 20-21). For instance when examining the results with a five year lag incorporated an ERR/100 WLM of 0.87 (95% CI: 0.18-1.56) was observed for individuals less than 55 years old, which dropped to 0.38 (95% CI: 0.016-0.75) for miners in the highest age category

of 75 years or older, with a slight increase in the ERR/100 WLM observed for miners 60-<65 years old (ERR/100 WLM=1.36, 95% CI: 0.76-1.96).

Table 20: Excess relative risk (ERR) of lung cancer mortality by attained age for male miners, no lag applied

Attained Age	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<55	160	0.80	0.14-1.45	0.04
55-<60	185	0.74	0.25-1.23	
60-<65	237	1.33	0.74-1.91	
65-<70	261	0.34	0.026-0.65	
70-<75	215	0.48	0.11-0.85	
75+	172	0.38	0.015-0.75	

[a]To test for homogeneity of ERR/WLM

Table 21: Excess relative risk (ERR) of lung cancer mortality by attained age for male miners, 5-year lag applied

Attained Age	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<55	160	0.87	0.18-1.56	0.03
55-<60	185	0.76	0.26-1.26	
60-<65	237	1.36	0.76-1.96	
65-<70	261	0.34	0.0295-0.66	
70-<75	215	0.49	0.12-0.86	
75+	172	0.38	0.016-0.75	

[a]To test for homogeneity of ERR/WLM

5.2.3 Exposure rate

There was an inverse relationship observed between the ERR/100 WLM and exposure rate (Tables 22-23). When a five year lag periods was incorporated into the calculation of cumulative exposure, the ERR/100 WLM was 3.08 (95% CI: 0.56-5.60) for exposure rate less than 2 WLM/yr compared to an ERR/100 WLM of 0.58 (95% CI: 0.36-0.81) for an exposure rate greater than 10 WLM/yr. The test of homogeneity was statistically significant ($p<0.001$).

Table 22: Excess relative risk (ERR) of lung cancer mortality by exposure rate for male miners, no lag applied

Exposure rate (WLM/yr)	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<2	344	2.81	0.46-5.15	<0.001
2-<5	238	1.60	0.75-2.45	
5-<10	333	1.27	0.74-1.80	
10+	315	0.54	0.32-0.76	

[a]To test for homogeneity of ERR/WLM

Table 23: Excess relative risk (ERR) of lung cancer mortality by exposure rate for male miners, 5-year lag applied

Exposure rate (WLM/yr)	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<2	343	3.08	0.56-5.60	<0.001
2-<5	239	1.81	0.88-2.73	
5-<10	327	1.20	0.67-1.74	
10+	321	0.58	0.36-0.81	

[a]To test for homogeneity of ERR/WLM

5.2.4 Time since first exposure

The ERR/100 WLM decreased with increasing time since first exposure (Tables 24-25). The ERR/100 WLM was 1.20 (95% CI: (-0.078)-2.50) for less than 15 years since first exposure and dropped to 0.14 (95% CI: (-0.16)-0.45) for more than 45 years since exposure with a five year lag incorporated into the calculation of cumulative exposure. The test of homogeneity was borderline significant (p=0.03).

Table 24: Excess relative risk (ERR) of lung cancer mortality by time since first exposure for male miners, no lag applied

Time since first exposure (years)	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<15	120	0.83	(-0.18)-1.80	0.04
15-<25	196	1.09	0.52-1.70	
25-<30	197	1.00	0.46-1.60	
30-<35	178	0.88	0.40-1.40	
35-<40	191	0.52	0.14-0.91	
40-<45	172	0.58	0.18-0.97	
>45	176	0.14	(-0.16)-0.44	

[a]To test for homogeneity of ERR/WLM

Table 25: Excess relative risk (ERR) of lung cancer mortality by time since first exposure for male miners**, 5-year lag applied**

Time since first exposure (years)	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<15	120	1.20	(-0.078)-2.50	0.03
15-<25	196	1.10	0.54-1.70	
25-<30	197	1.00	0.45-1.60	
30-<35	178	0.90	0.41-1.40	
35-<40	191	0.53	0.14-0.91	
40-<45	172	0.58	0.18-0.98	
>45	176	0.14	(-0.16)-0.45	

[a]To test for homogeneity of ERR/WLM

5.2.5 Time since last exposure

There were statistically significant changes in the ERR/100 WLM across categories of time since last exposure ($p<0.001$) (Table 26-27). The ERR/100 WLM was 1.42 (95% CI: 0.93-1.91) (five year lag incorporated into cumulative exposure) for less than 15 years since last exposure, which dropped to 0 ERR/WLM with longest time since last exposure ($\geq$ 40 years).

Table 26: Excess relative risk (ERR) of lung cancer mortality by time since last exposure for male miners**, no lag applied**

Time since last exposure (years)	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<15	268	1.34	0.87-1.82	<0.001
15-<25	274	0.86	0.48-1.24	
25-<30	200	0.80	0.33-1.27	
30-<40	275	0.12	(-0.14)-0.38	
≥ 40	213	(-0.0036)	(-0.32)-0.32	

[a]To test for homogeneity of ERR/WLM

Table 27: Excess relative risk (ERR) of lung cancer mortality by time since last exposure for male miners, 5-year lag applied

Time since last exposure (years)	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<15	268	1.42	0.93-1.91	<0.001
15-<25	274	0.87	0.49-1.25	
25-<30	200	0.81	0.33-1.28	
30-<40	275	0.12	(-0.13)-0.38	
≥ 40	213	0.00	(-0.32)-0.32	

[a]To test for homogeneity of ERR/WLM

5.2.6 Age at first exposure

The ERR/100 WLM increased with an increase in the age at first exposure (Table 28-29). The ERR/100 WLM for age at first exposure younger than 25 years is 0.27 (95% CI: -0.022-0.56) and increased three-fold to 0.81 (95% CI: 0.44-1.18) for those older than 35 years at first exposure with a five year lag applied.

Table 28: Excess relative risk (ERR) of lung cancer mortality by age at first exposure for male miners**, no lag applied**

Age at first exposure	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<25	300	0.26	(-0.027)-0.55	0.03
≥25-30	259	0.76	0.40-1.12	
≥30-35	266	0.90	0.50-1.31	
≥35	405	0.76	0.40-1.11	

[a]To test for homogeneity of ERR/WLM

Table 29: Excess relative risk (ERR) of lung cancer mortality by age at first exposure for male miners**, 5-year lag applied**

Age at first exposure	Lung cancer deaths	ERR/100 WLM	95% CI	P-value[a]
<25	300	0.27	(-0.022)-0.56	0.02
≥25-30	259	0.75	0.39-1.12	
≥30-35	266	0.93	0.52-1.35	
≥35	405	0.81	0.44-1.18	

[a]To test for homogeneity of ERR/WLM

5.2.7 Inverse dose-rate

In examining the inverse dose-rate effect (Table 30), within higher cumulative exposures (>40 WLM) a linear positive dose-response relationship was clearly observed between duration of exposure and lung cancer risk (p <0.0001). Within the cumulative exposure category >5-40 WLM, although the linear trend was statistically significant (p<0.0001), a monotonic increase in the dose-response relationship was not observed with duration of exposure due to the drop in the relative risk in the highest duration category (<10 years of exposure). A significant dose-response relationship was not evident within the lowest cumulative exposure category <5 WLM (p=0.24).

Table 30: Relative risk of lung cancer mortality by duration of exposure within lifetime cumulative dose categories for male miners

Lifetime Cumulative WLM		Duration of exposure (years)				P value
		<3	3-<5	5-<10	> 10	
WLM: <5	Cases	293	37	13	0	
	RR	1.00	1.16 (0.82-1.64)	0.75 (0.43-1.31)	-	0.24
WLM: >5-40	Cases	204	178	78	34	
	RR	1.00	1.36 (1.11-1.66)	1.82 (1.40-2.37)	1.34 (0.92-1.95)	<0.0001
WLM: >40	Cases	10	70	181	132	
	RR	1.00	1.21 (0.63-2.36)	1.50 (0.79-2.84)	2.46 (1.29-4.68)	<0.0001

5.3 Radon exposure and lung cancer incidence

Tables 31-32 and Figure 9 present the risk of lung cancer incidence with increasing cumulative radon exposure for no lag and with a five year lag applied. Several different lag periods (five, 10, 15 and 20) were assessed and, as per Rothman's principle, the five year lag period was chosen because it yielded the highest risk estimates. Similar to lung cancer mortality, there was a dose-response relationship between cumulative radon exposure and lung cancer incidence. Workers in the highest category with over 100 WLM of cumulative radon exposure had just under a two-fold increase in the risk of lung cancer compared to the unexposed group (RR=1.89, 95% CI: 1.43-2.50). Using the continuous WLM, the excess relative risk estimate was 0.63/100 WLM (95% CI: 0.42-0.84) with no lag applied; and 0.64/100 WLM (95% CI: 0.43-0.85) with a five-year lag incorporated into the calculation of cumulative exposure, while adjusting for age and calendar period (Figure 9).

Table 31: Lung cancer incidence by cumulative exposure to radon progeny in working level months (WLM) among male miners, with no lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer cases	RR[b]	95% CI
0	0	50450	63	1	*
>0-1	0.36	161683	125	1.05	0.77-1.42
>1-5	2.63	166689	165	0.93	0.69-1.24
>5-10	7.22	102804	124	0.82	0.6-1.11
>10-20	14.3	114725	185	0.95	0.72-1.27
>20-30	24.4	54052	120	1.15	0.85-1.56
>30-50	38.5	58481	148	1.2	0.89-1.62
>50-100	70.1	52182	170	1.42	1.06-1.90
>100	164.3	40660	174	1.82	1.36-2.43

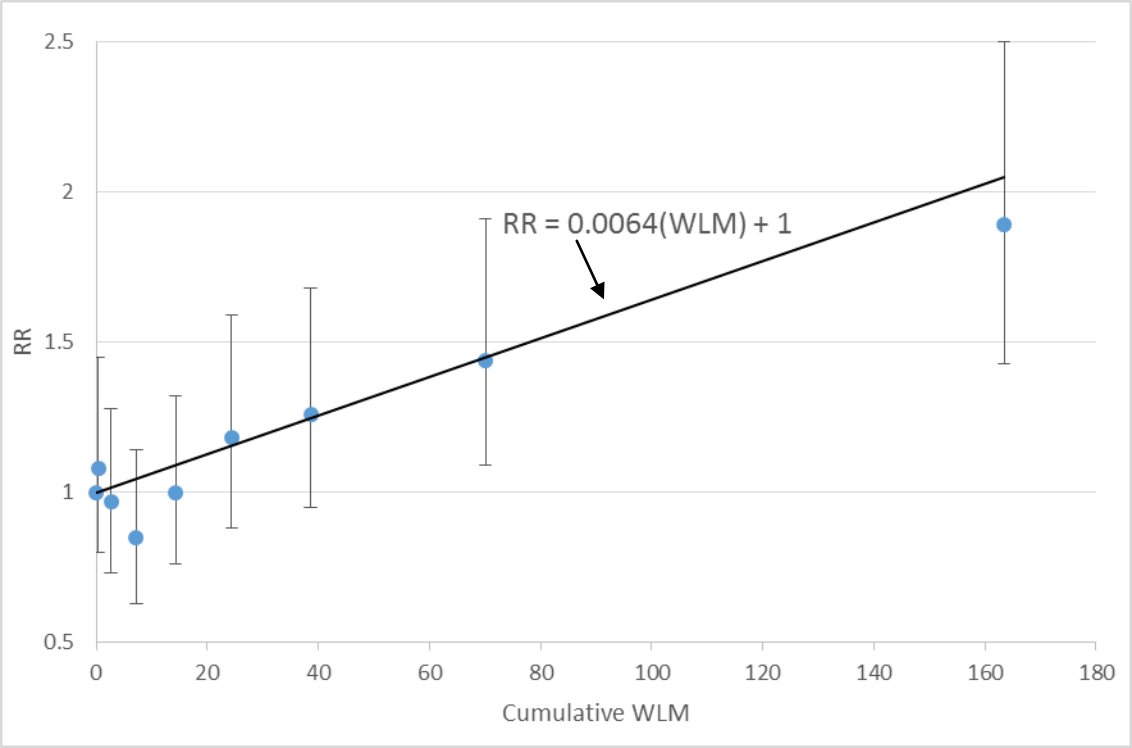
* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Table 32: Lung cancer incidence by cumulative exposure to radon progeny in working level months (WLM) among male miners, with five-year lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer cases	RR[b]	95% CI
0	0	114775	69	1	*
>0-1	0.36	135277	120	1.08	0.80-1.45
>1-5	2.64	148594	165	0.97	0.73-1.28
>5-10	7.22	94983	124	0.85	0.63-1.14
>10-20	14.3	107215	186	1.00	0.76-1.32
>20-30	24.4	51715	119	1.18	0.88-1.59
>30-50	38.6	57403	150	1.26	0.95-1.68
>50-100	70.1	51705	167	1.44	1.09-1.91
>100	163.5	40058	174	1.89	1.43-2.50

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Figure 9: Relative risk of lung cancer incidence by cumulative exposure to radon and ERR/WLM, with a five year lag applied



In comparing results between lung cancer mortality and incidence, a similar dose response relationship was observed with cumulative exposure to radon. Although risk estimates in each exposure category appeared higher for lung cancer mortality, the 95% confidence intervals overlapped with those for lung cancer incidence suggesting that the values are comparable. However, in comparing these results it should be noted that the period of follow-up available for mortality (1954-2007) and cancer incidence (1969-2005) were slightly different.

Modifying Factors

Results for testing the impact of various modifying factors on the risk of lung cancer incidence are presented below for no lag and five year lag applied. Several different lag periods (five, 10, 15 and 20) were assessed and, as per Rothman's principle, the five year lag period was chosen because it yielded the highest risk estimates. The various modifying factors followed the same trends found for lung cancer mortality where there was an inverse relationship observed between the ERR/100 WLM and exposure rate, time since first exposure and time since last exposure with a statistically significant test of homogeneity (Tables 33-42). Although an inverse relationship was observed for attained age and ERR/ 100 WLM, the test of homogeneity was not statistically significant (p=0.08). A positive relationship was observed between ERR/100 WLM and age at first exposure, although the test of homogeneity was also not statistically significant (p=0.32 (for five-year lag incorporated)).

5.3.1 Attained Age

Table 33: Excess relative risk (ERR) of lung cancer incidence by attained age for male miners, no lag applied

Age at first exposure	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<55	188	0.99	0.31-1.68	0.09
55-<60	204	0.72	0.26-1.17	
60-<65	251	1.05	0.55-1.54	
65-<70	273	0.43	0.11-0.75	
70-<75	214	0.54	0.15-0.92	
75+	144	0.23	(-0.12)-0.57	

[a]To test for homogeneity of ERR/WLM

Table 34: Excess relative risk (ERR) of lung cancer incidence by attained age for male miners, 5-year lag applied

Age at first exposure	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<55	188	1.00	0.33-1.70	0.08
55-<60	204	0.71	0.25-1.16	
60-<65	251	1.05	0.0055-1.55	
65-<70	273	0.44	0.12-0.76	
70-<75	214	0.54	0.15-0.92	
75+	144	0.23	(-0.12)-0.58	

[a]To test for homogeneity of ERR/WLM

5.3.2 Exposure rate

Table 35: Excess relative risk (ERR) of lung cancer incidence by exposure rate for male miners, no lag applied

Exposure rate (WLM/yr)	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<2	354	3.02	0.65-5.39	<0.001
2-<5	247	1.38	0.59-2.18	
5-<10	350	1.37	0.83-1.90	
10+	323	0.53	0.31-0.74	

[a]To test for homogeneity of ERR/WLM

Table 36: Excess relative risk (ERR) of lung cancer incidence by exposure rate for male miners, 5-year lag applied

Exposure rate (WLM/yr)	Lung cancer cases	ERR/ 100 WLM	95% CI	P-value[a]
<2	352	3.46	0.86-6.05	<0.001
2-<5	246	1.50	0.65-2.35	
5-<10	347	1.30	0.77-1.83	
10+	329	0.56	0.34-0.78	

[a]To test for homogeneity of ERR/WLM

5.3.3 Time since first exposure

Table 37: Excess relative risk (ERR) of lung cancer incidence by time since first exposure for male miners, no lag applied

Time since first exposure (years)	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<15	116	1.21	(-0.46)-2.87	0.01
15-<25	220	1.04	0.51-1.58	
25-<30	202	0.85	0.36-1.33	
30-<35	204	0.99	0.53-1.45	
35-<40	214	0.42	0.079-0.77	
40-<45	182	0.55	0.17-0.92	
>45	136	0.072	(-0.24)-0.39	

[a]To test for homogeneity of ERR/WLM

Table 38: Excess relative risk (ERR) of lung cancer incidence by time since first exposure for male miners, 5-year lag applied

Time since first exposure (years)	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<15	116	1.39	(-0.42)-3.21	0.01
15-<25	220	1.06	0.52-1.61	
25-<30	202	0.85	0.36-1.34	
30-<35	204	0.99	0.53-1.45	
35-<40	214	0.42	0.080-0.77	
40-<45	182	0.55	0.17-0.92	
>45	136	0.073	(-0.24)-0.39	

[a]To test for homogeneity of ERR/WLM

5.3.4 Time since last exposure

Table 39: Excess relative risk (ERR) of lung cancer incidence by time since last exposure for male miners, no lag applied

Time since last exposure (years)	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<15	294	1.34	0.89-1.80	<0.001
15-<25	292	0.78	0.43-1.12	
25-<30	187	0.57	0.16-0.98	
30-<40	313	0.20	(-0.058)-0.45	
≥ 40	188	(-0.031)	(-0.38)-0.32	

[a]To test for homogeneity of ERR/WLM

Table 40: Excess relative risk (ERR) of lung cancer incidence by time since last exposure for male miners, 5-year lag applied

Time since last exposure (years)	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<15	294	1.37	0.91-1.84	<0.001
15-<25	292	0.78	0.43-1.13	
25-<30	187	0.58	0.16-0.99	
30-<40	313	0.20	(-0.057)-0.46	
≥ 40	188	(-0.030)	(-0.38)-0.32	

[a]To test for homogeneity of ERR/WLM

5.3.5 Age at first exposure

Table 41: Excess relative risk (ERR) of lung cancer incidence by age at first exposure for male miners, no lag applied

Age at first exposure	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<25	327	0.40	0.091-0.70	0.33
≥25-30	278	0.74	0.39-1.09	
≥30-35	264	0.73	0.36-1.10	
≥35	405	0.71	0.37-1.05	

[a]To test for homogeneity of ERR/WLM

Table 42: Excess relative risk (ERR) of lung cancer incidence by age at first exposure for male miners, 5-year lag applied

Age at first exposure	Lung cancer cases	ERR/100 WLM	95% CI	P-value[a]
<25	327	0.4	0.09-0.70	0.32
≥25-30	278	0.75	0.4-01.11	
≥30-35	264	0.74	0.36-1.11	
≥35	405	0.72	0.38-1.06	

[a]To test for homogeneity of ERR/WLM

5.4 Radon exposure and lung cancer morphology

Morphology code was available for 1,256 cases out of the total 1,274 lung cancer cases. The morphology codes were grouped into the following categories: squamous cells, adenocarcinoma, large cells, small cells and other/unspecified (Table 43). Squamous cells were the predominant cell type (37% of lung cancers with known morphology), followed by adenocarcinoma (24% of known lung cancers) (Table 44).

Table 43: Distribution of lung cancer cases by histology

Lung cancer histology	ICD codes	Number of cases
Squamous cells	8050-8053, 8060, 8070-8078, 8083-8084	391
Adenocarcinoma	8140, 8211, 8230-8231, 8250-8260, 8323, 8480-8481, 8490, 8550-8551, 8570-8574, 8576	249
Large cells	8010-8012, 8014, 8015, 8020, 8021, 8022, 8030, 8031, 8035, 8310, 8046	225
Small cells	8041-8045	181
Unspecified/Other	Other specified carcinoma (8246), sarcoma (8800- 8811, 8830, 8840-8921, 8990-8991, 9040-9044, 9120-9133, 9150, 9540-9581), unspecified (8000-8005)	210
Total		1,256

Table 44: Distribution of lung cancer histology by categories of cumulative exposure

Cumulative exposure (WLM)	Squamous cell	Adenocarcinoma	Large cell	Small cell	Total
<1	49	44	36	27	156
1-10	86	61	56	35	238
>10-20	52	44	27	26	149
>20-60	98	57	55	47	257
>60	106	43	51	46	246
Row Total (%)	391 (37%)	249 (24%)	225 (22%)	181 (17%)	1046 (100%)

The large sample size allowed an investigation of the dose-response relationship for the four major morphological groups (Tables 45-52) for no lag and with a five year lag applied. For comparison Tables 53 and 54 present the results of the dose-response analyses for all incident lung cancer cases using similar cumulative exposure categories. Figure 10 provides a comparison of the dose-response relationship between the four morphological groups. Several different lag periods (5, 10, 15 and 20) were assessed, and results were similar across each one. Thus the five year lag was applied to be consistent with results for overall lung cancer incidence presented above. In examining the distribution of lung cancer histology by cumulative exposure, a larger proportion of the cases in the highest dose category (>60 WLM) were squamous cells carcinoma, whereas in the lowest dose category (<1 WLM) an equally large proportion of cases were squamous cell carcinoma and adenocarcinoma (~25%) (Table 44).

A clear dose-response relationship was observed between cumulative radon exposure and both squamous cell and small cell carcinoma incidence. The relative risk for squamous cell carcinoma and small cell carcinoma appeared higher across cumulative radon exposure categories compared to the other morphological groups and all cases combined. In particular the risk was higher in the highest dose categories (>20 WLM and >60 WLM) where the risk of both squamous and small cells was two-fold higher than the respective reference groups (<1 WLM). For the adenocarcinomas, there were no significant excesses observed for any of the cumulative dose categories. For large cells, there was a 55% increase in the risk observed in the highest dose category (>60 WLM).

Table 45: Lung cancer incidence for squamous cells by cumulative exposure to radon progeny in working level months (WLM) for male miners, no lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	209644	49	1	*
1-10	271982	86	0.92	0.65-1.31
>10-20	114725	52	0.93	0.63-1.38
>20-60	128757	98	1.27	0.90-1.80
>60	76618	106	2.02	1.43-2.85

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 46: Lung cancer incidence for squamous cells by cumulative exposure to radon progeny in working level months (WLM) for male miners, 5-year lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	247983	50	1	*
1-10	245646	85	0.92	0.65-1.31
>10-20	107215	52	0.94	0.64-1.39
>20-60	125152	98	1.28	0.90-1.81
>60	75730	106	2.03	1.44-2.86

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 47: Lung cancer incidence for adenocarcinoma by cumulative exposure to radon progeny in working level months (WLM) for male miners, no lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	209644	44	1	*
1-10	271982	61	0.81	0.55-1.20
>10-20	114725	44	1.05	0.68-1.60
>20-60	128757	57	1.02	0.68-1.53
>60	76618	43	1.18	0.76-1.82

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 48: Lung cancer incidence for adenocarcinoma by cumulative exposure to radon progeny in working level months (WLM) for male miners, 5-year lag applied

Cumulative exposure	PYAR	# of cases	RR[a]	95% CI

(WLM)				
<1	247983	44	1	*
1-10	245646	62	0.87	0.59-1.28
>10-20	107215	43	1.07	0.70-1.64
>20-60	125152	57	1.07	0.71-1.60
>60	75730	43	1.23	0.79-1.90

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 49: Lung cancer incidence for large cells by cumulative exposure to radon progeny in working level months (WLM) for male miners, no lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	209644	36	1	*
1-10	271982	56	0.86	0.57-1.31
>10-20	114725	27	0.72	0.44-1.19
>20-60	128757	55	1.08	0.70-1.66
>60	76618	51	1.50	0.97-2.32

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 50: Lung cancer incidence for large cells by cumulative exposure to radon progeny in working level months (WLM) for male miners, 5 year lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	247983	36	1	*
1-10	245646	56	0.89	0.58-1.36
>10-20	107215	27	0.74	0.45-1.23
>20-60	125152	55	1.11	0.72-1.71
>60	75730	51	1.55	0.99-2.41

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 51: Lung cancer incidence for small cells by cumulative exposure to radon progeny in working level months (WLM) for male miners, no lag applied

Cumulative exposure	PYAR	# of cases	RR[a]	95% CI

(WLM)				
<1	209644	27	1	*
1-10	271982	35	0.75	0.46-1.25
>10-20	114725	26	1.00	0.58-1.73
>20-60	128757	47	1.36	0.83-2.21
>60	76618	46	2.01	1.23-3.29

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 52: Lung cancer incidence for small cells by cumulative exposure to radon progeny in working level months (WLM) for male miners, 5-year lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	247983	27	1	*
1-10	245646	35	0.81	0.48-1.34
>10-20	107215	27	1.11	0.64-1.90
>20-60	125152	46	1.40	0.86-2.29
>60	75730	46	2.12	1.29-3.48

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Table 53: Lung cancer incidence for all cases by cumulative exposure to radon progeny in working level months (WLM) for male miners, no lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI
<1	209644	187	1	*
1-10	271982	290	0.85	0.70-1.02
>10-20	114725	185	0.92	0.75-1.13
>20-60	128757	315	1.15	0.95-1.38
>60	76618	297	1.61	1.33-1.94

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

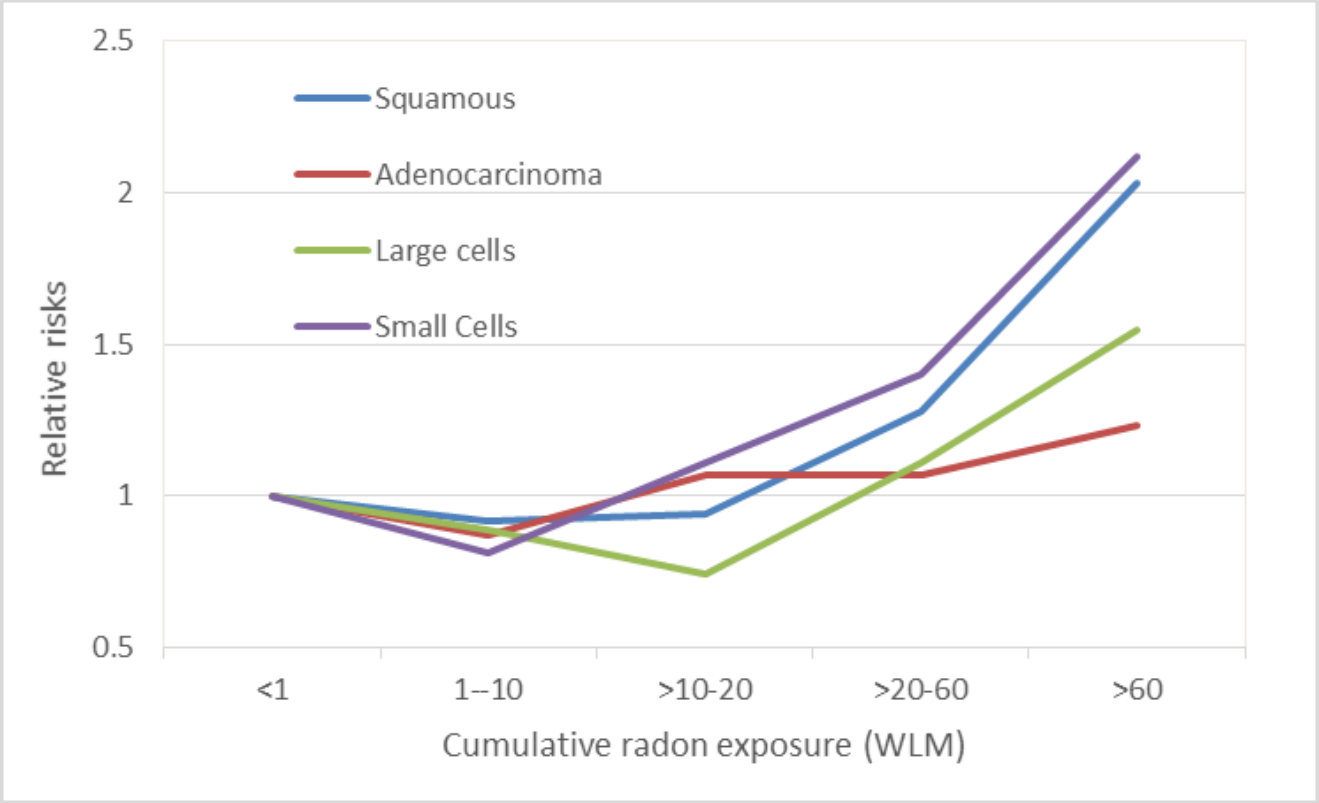
Table 54: Lung cancer incidence for all cases by cumulative exposure to radon progeny in working level months (WLM) for male miners, 5 year lag applied

Cumulative exposure (WLM)	PYAR	# of cases	RR[a]	95% CI

<1	247983	188	1	*
1-10	245646	290	0.87	0.72-1.04
>10-20	107215	186	0.95	0.77-1.16
>20-60	125152	313	1.17	0.97-1.40
>60	75730	297	1.64	1.36-1.98

* Referent group
[a] Relative risks were adjusted for attained age and calendar period

Figure 10: Relative risk of lung cancer by morphology group from cumulative exposure to radon, with a five year lag applied



5.5 Examination of risks among modern miners

There were only 198 cases of lung cancer deaths among 13, 277 modern miners (miners who started employment after 1970 when ventilation practices were introduced). The categories for cumulative

radon exposure were chosen to be comparable to categories chosen for the entire cohort. Miners who started employment after 1970 (Tables 55-56) had similar risks of lung cancer mortality to the full cohort for the same categories, although the risk was lower in some categories. For instance, in the highest cumulative category of >5 WLM with a five year lag period modern miners did not have an elevated risk of lung cancer mortality (RR=1.10, 95% CI: 0.67-1.81). However, the small sample size available may not provide stable estimates of the true relative risks and provides insufficient power to detect an effect if it exists.

Table 55: Lung cancer mortality among male miners who started employment in 1970 or later by cumulative exposure to radon progeny in working level months (WLM), no lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer deaths	RR[b]	95% CI
0	0	37702	29	1	*
>0-1	0.33	149825	98	1.22	0.80-1.84
>1-5	2.5	101511	36	0.86	0.52-1.41
>5	12.1	81657	35	0.93	0.57-1.54

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Table 56: Lung cancer mortality among male miners who started employment in 1970 or later by cumulative exposure to radon progeny in working level months (WLM), 5-year lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer deaths	RR[b]	95% CI
0	0	96460	31	1	*
>0-1	0.33	124469	97	1.41	0.93-2.13
>1-5	2.5	84422	35	0.96	0.59-1.57
>5	11.9	65344	35	1.1	0.67-1.81

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

5.6 Exploratory analyses of RDP exposure and cancer incidence and mortality for cancers other than lung

Other than lung cancer there are very few cancer sites that have limited evidence for an association with radon exposure. Results for other cancer sites including stomach and leukemia are presented

below in Tables 57-59 with a lag interval of 2 years and 10 years for stomach and leukemia, respectively, applied to cumulative radon exposure, which yielded the highest risk estimates for these cancer sites. Overall, there were no clear dose-response relationships observed with any of these cancer sites. Using the continuous WLM, the excess relative risk estimate was -0.00065 (95% CI: (-0.0060)-0.0047) for stomach cancer mortality and 0.0007 (95% CI: (-0.0068)-0.0082) for leukemia mortality.

Table 57: Stomach cancer mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, 2 year lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer deaths	RR[b]	95% CI
≤ 2	0.46	347768	22	1	*
>2-≤10	5.32	244639	29	1.18	0.67-2.06
>10-≤30	17.6	212082	25	0.91	0.51-1.63
>30	81.4	194102	32	1.00	0.57-1.74

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Table 58: Leukemia mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, 10 year lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer deaths	RR[b]	95% CI
≤ 5	0.73	586559	28	1	*
>5-30	13.8	260061	29	1.17	0.68-2.04
>30	80.7	151971	20	1.12	0.61-2.08

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Table 59: Stomach cancer incidence by cumulative exposure to radon progeny in working level months (WLM) among male miners, 2 year lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Lung cancer deaths	RR[b]	95% CI
≤ 2	0.49	286199	29	1	*
>2-≤10	5.27	200184	32	1.01	0.61-1.68
>10-≤30	17.5	165260	28	0.80	0.47-1.35

>30	83.2	151124	35	0.87	0.52-1.44

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

5.7 Exploratory analyses of RDP exposure and non-cancer mortality

The relationship between RDP exposure and cardiovascular disease mortality are presented in Table 60 with a 10 year lag applied to the calculation of cumulative exposure. Several different lag periods (five, 10, 15 and 20) were assessed and, as per Rothman's principle, the ten year lag period was chosen because it yielded the highest risk estimates. There was no clear dose-response relationship observed. Using the continuous WLM, the excess relative risk estimate with a 10 year lag interval applied was 0.00065 (95% CI: (-0.00041)-0.0017).

Table 60: Cardiovascular disease mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, 10 year lag applied

Cumulative exposure (WLM)	Mean cumulative exposure (WLM)[a]	Person-years	Cardiovascular deaths	RR[b]	95% CI
0	0	323239	274	1	
>0-2	0.70	171574	395	1.10	0.93-1.29
>2-7	4.21	136981	428	1.07	0.91-1.25
>7-20	12.4	159877	563	0.97	0.83-1.13
>20-50	31.9	114330	525	1.09	0.93-1.27
>50	108.6	91204	496	1.10	0.94-1.29

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

5.8 Sensitivity Analysis Assessing Different Sources of Exposure Data

Figure 11 demonstrates the mean radon exposure over time when favoring exposure data from the MMF over the NDR compared to the approach used in the current study which favored the NDR over the MMF where a miner had doses available in both. Based on Figure 11, the mean radon

exposure for Ontario miners was of similar magnitude for both approaches and the general trend over time was also comparable, with a peak in exposure seen in the early 1960s and then a steady decline seen subsequently. Tables 61-62 present the risk estimates derived when favoring the MMF over the NDR. In comparing these results to Tables 18-19, where the NDR was favored over the MMF, the overall dose-response relationship observed with lung cancer mortality was similar. For instance, a two-fold excess was still observed in the highest dose category (>100 WLM, RR: 2.42, 95% CI: 1.80-3.25) with a five year lag applied.

Figure 11: Mean annual radon exposure from 1954-1996 favoring different sources of exposure data

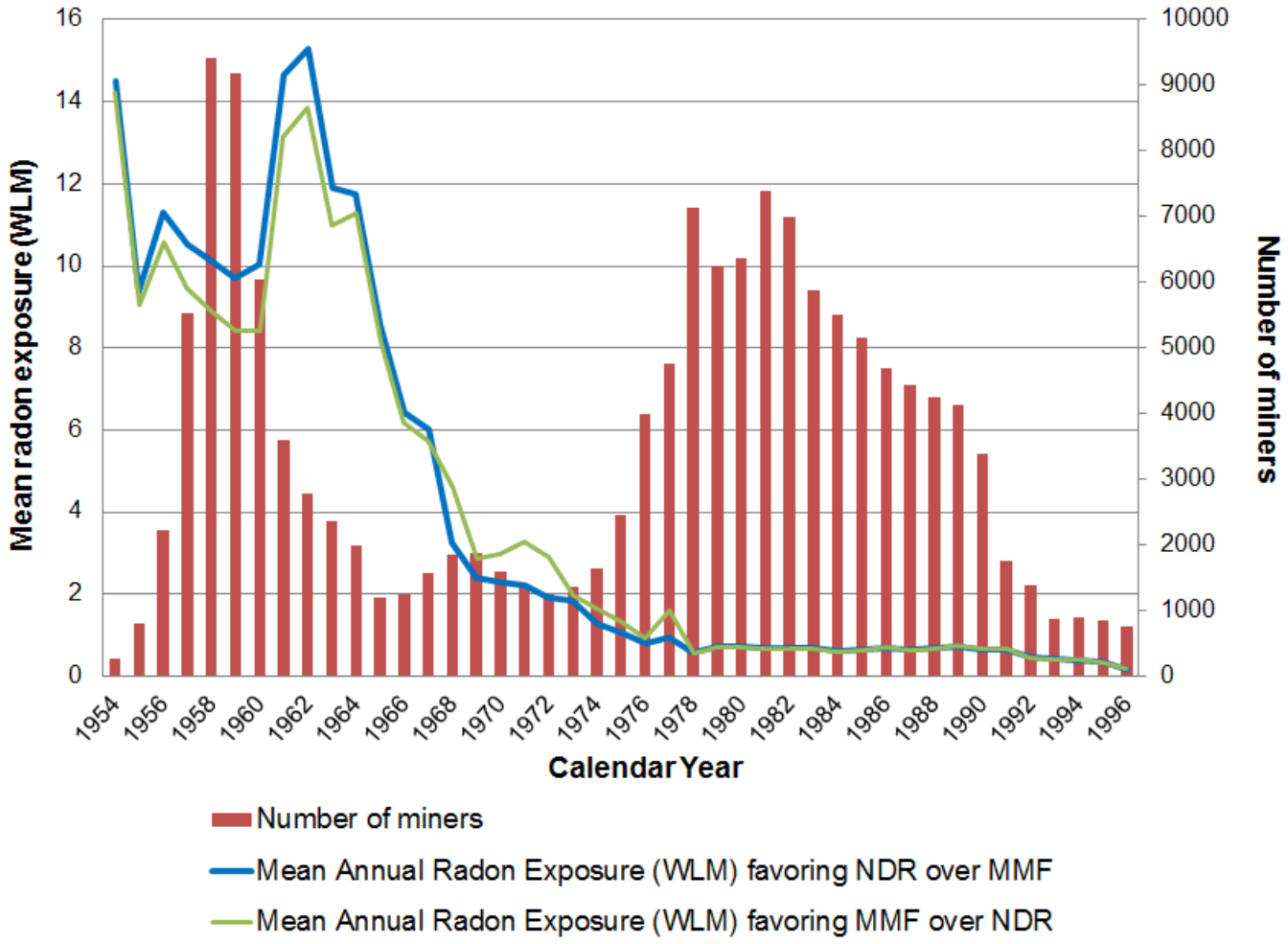


Table 61: Lung cancer mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, favoring MMF over the NDR, no lag applied

Cumulative exposure (WLM)	Mean exposure (WLM)[a]	Person-years	Lung cancer deaths	Relative Risk[b]	95% CI
0	0	64792	57	1	*
>0-1	0.37	172595	127	1.30	0.95-1.78
>1-5	2.67	211013	172	1.04	0.77-1.41
>5-10	7.23	138991	145	1.08	0.79-1.46
>10-20	14.3	153745	180	1.11	0.82-1.49
>20-30	24.4	70806	113	1.35	0.98-1.85
>30-50	38.3	76057	137	1.43	1.05-1.95
>50-100	70.1	65783	148	1.62	1.19-2.20
>100	163.8	44808	151	2.20	1.62-2.98

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

Table 62: Lung cancer mortality by cumulative exposure to radon progeny in working level months (WLM) among male miners, favoring MMF over the NDR, 5 year lag applied

Cumulative exposure (WLM)	Mean exposure (WLM)[a]	Person-years	Lung cancer deaths	Relative Risk[b]	95% CI
0	0	196449	63	1	*
>0-1	0.37	144596	126	1.44	1.06-1.96
>1-5	2.67	181149	171	1.14	0.85-1.52
>5-10	7.23	120206	145	1.18	0.88-1.59
>10-20	14.3	132702	181	1.22	0.91-1.63
>20-30	24.4	61378	113	1.47	1.08-2.01
>30-50	38.3	66304	135	1.54	1.14-2.08
>50-100	70.1	57289	146	1.75	1.30-2.36
>100	163.4	38517	150	2.42	1.80-3.25

* Referent group
[a] Means were weighted by person-years
[b] Relative risks were adjusted for attained age and calendar period

6. DISCUSSION

This study confirms what is known about underground uranium miners, which is that they have an increased risk of lung cancer. An increasing risk of lung cancer was also observed with cumulative radon exposures, particularly greater than 50 WLM. The excess relative risk per 100 WLM was 0.66 (95% CI: 0.44-0.87) for lung cancer mortality and 0.64 (95% CI: 0.43-0.85) for lung cancer incidence. A past update of this cohort observed an excess relative risk per WLM of 0.015 for lung cancer mortality (63).

In examining various modifying factors, the association between lung cancer mortality and radon exposure was modified by attained age, age at first exposure, time since last exposure, time since first exposure and exposure rate. For lung cancer incidence, the relationship with radon was strongly modified by exposure rate, time since first exposure and time since last exposure. An inverse relationship was observed with attained age, which was stronger for lung cancer mortality than lung cancer incidence. Similarly, the BEIR VI report found decreasing excess relative risks with attained age (22), which has also been seen in other studies including the 1994 Lubin et al. pooled analysis of 11 cohorts (56). The pooled results found a greater excess relative risk with the <50 age group and dropped considerably in the $\underline{\geq}$ 75 age group. Likewise, we observed a greater excess relative risk with the >55 age group, our lowest age group, which declined in the $\underline{\geq}$ 75 age group. The most recent prior update of this Ontario cohort also found similar trends for attained age (14). For time since first and last exposure, our results demonstrated a decrease in the excess relative risk with increasing time since exposure. The BEIR models also demonstrated a declining dose-response relationship with increasing time since exposure(20, 22). Similarly, results from the latest update of the Czech cohort found a strong inverse dose-response relationship with time since exposure(48). Age at first exposure

also modified the dose-response relationship for lung cancer mortality in our study. However, there is limited evidence from other studies that age at first exposure modifies the dose-response relationship including the direction of this modification. For instance, significant variations in the ERR/WLM were observed in the China cohort, whereby the risks decreased with increasing age at first exposure, while in the Czech cohort the reverse association was seen, whereby risks increased. However, in the combined analysis of 11 cohorts, Lubin et al. did not find age at first exposure to be an important modifier of lung cancer risks.

In examining the inverse dose-rate effect it was observed that within the high cumulative radon exposure category the risk of lung cancer mortality was higher with longer periods of exposure. The biological explanation for this phenomenon has been explored in previous literature (16, 80), the basis of which is that with an extended dose, more cells are targeted when they are in the most susceptible part of the cell cycle, whereby mutations can occur. However, if the dose-rate or cumulative dose is too low, this will not allow enough susceptible cells to be targeted over time and the inverse dose rate effect is no longer apparent. Using pooled data from 11 miner cohort studies, Lubin et al. 1995 conducted an analysis of the inverse dose-rate effect at low doses (16). The study noted that for cumulative exposure less than 50 WLM the inverse dose-rate effect starts to disappear. Similarly, Brenner 1994 (80) observed that 50 WLM represents an appropriate cut point between low and high exposures sufficient to provide multiple hits to susceptible cells. However, due to the linear nature of the relationship, 50 WLM may still be an arbitrary cut point.

Our study found higher relative risks associated with the squamous cell and small cell carcinoma than for other histologic types. There is limited evidence that the histologic type is related specifically to radon induced lung cancer cases (22). A study of German miners evaluated radon

exposure and lung cancer risk by histopathology, and found a higher proportion of squamous cell carcinoma and small cell carcinoma among the higher radon exposure (81). Furthermore, there is evidence that smokers have a higher risk of developing squamous cell and small cell carcinoma (82). Unfortunately, the lack of smoking data in our study precluded us from examining if this may explain the higher risks associated with the squamous and small cell carcinoma seen in our study.

In exploring associations between cancers other than lung and radon exposure, no excesses or clear dose-response relationships were apparent for stomach cancer and leukemia. The most recent update of the German cohort also examined these cancers and saw a borderline increase in risk for stomach cancer (ERR/100 WLM=0.022; 95% CI: 0.001-0.042) and no risk with leukemia (ERR/100 WLM= 0.005 (95% CI: -0.034-0.045) (52). Similarly, no clear associations were seen with cardiovascular disease mortality and cumulative radon exposure. Several other cohorts that have examined cardiovascular diseases have also not observed an increased risk (7, 45, 52). Of the previous cohort studies, only the French observed an association between cumulative radon exposure and cerebrovascular disease (ERR/100WLM= 0.41, 95% CI: 0.04-1.03) (50).

Consistent with past Ontario and other uranium cohort studies lung cancer mortality and incidence rates were persistently elevated overall and across sub-cohorts (i.e., gold mining experience and mining region) relative to the general population. Other major elevations of interest in the cohort were silicosis mortality, which was also prominent in the ever-gold miners and Elliot Lake region sub-analyses, and is consistent with established concern in the history of Ontario uranium mining (83, 84). The silicosis elevations highlight the importance of silica as a potential confounder or effect modifier in the association between radon exposure and lung cancer risk. Addressing this concern in the cohort directly presents difficulties because there are insufficient measurements of

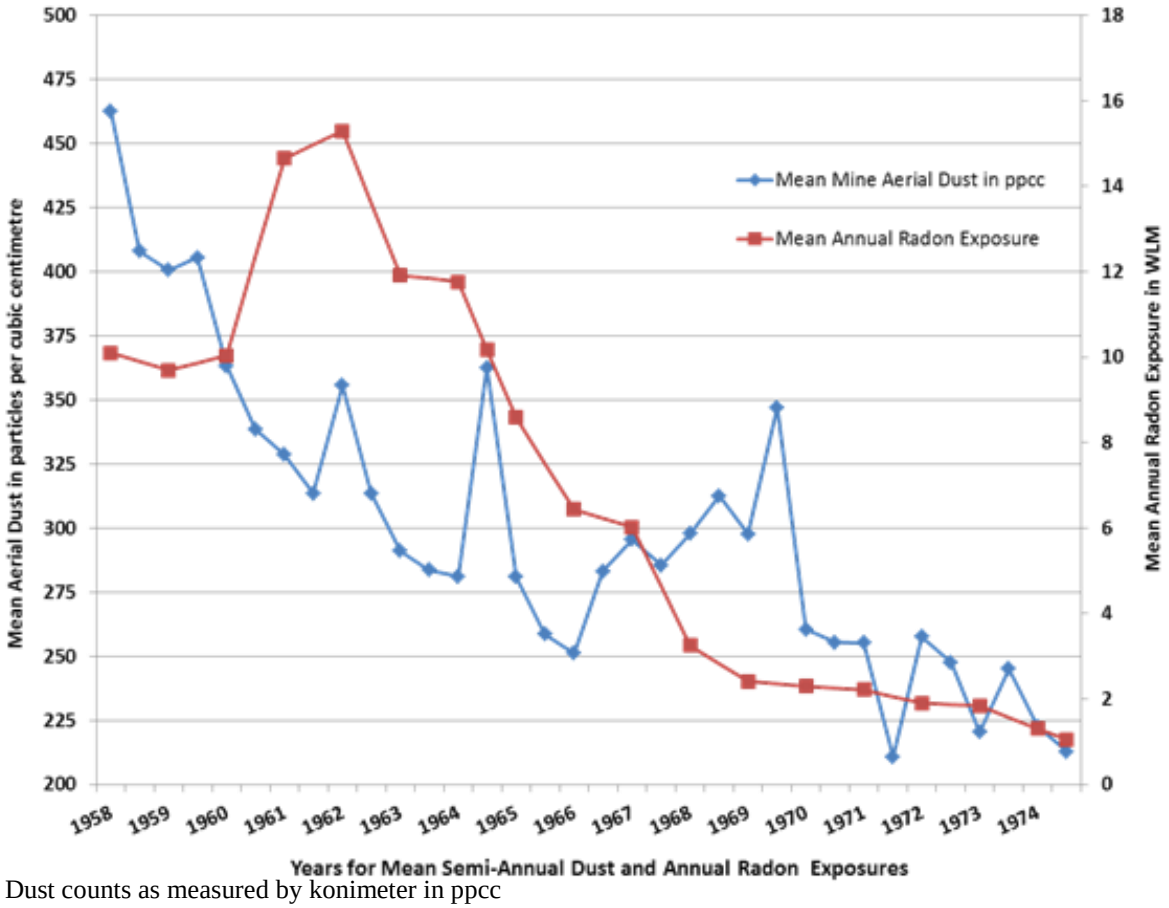
silica dust exposure available in order to adjust for confounding, though there are regional differences in the quartz content of ores between Elliot Lake and Bancroft region mines (11, 83, 84). Mean silica content in ores for Ontario uranium mining regions and overall gold and nickel mines can be found in the following Table 63 and weighted semi-annual mean aerial dust counts in particles per cubic centimetre (ppcc) for Ontario uranium mines is displayed in Figure 12 in relation to cohort radon exposures (11, 85).

Table 63: Mean dust levels and free crystalline silica ore by underground mine type

Ontario Mine Type And/or Region (11)	Percentage Range of Silica in Ores	1960 Mean Dust Level in air in ppcc	1975 Mean Dust Level in air in ppcc
Uranium – Elliot Lake	60 – 70%	400	220
Uranium - Bancroft	5 – 15%		
Gold	15 – 35%	400	250
Nickel	10%	680	310

ppcc = Dust levels in particles per cubic centimetre as measured by a konimeter
silica in ore = quartz in dust based on analysis of settled aerial dust
Mean Dust Levels were from combined Elliot Lake and Bancroft uranium mines

Figure 12: Semi-Annual Mean Ontario Uranium Mine Dust Counts and Radon Exposures, 1958-1975



Dust counts as measured by konimeter in ppcc
MAPAO Dust Survey Data Adapted from Ham Commission Report (11)

Present silicosis regional mortality results are consistent with previous Ontario uranium miner cohort updates (61, 63). There is, little known of the effects of concurrent quartz dust and radon exposures but the most recent study involving nearly fifty years of concurrent measurement of the two in the German Wismut uranium miner cohort (1946-2003) found an additive relationship with risk of lung cancer mortality (51).

Significantly increased death rates from accidents, poisoning and violence, were observed in the present cohort as well as across sub-cohorts and were consistent with past updates and other Northeastern Ontario underground miner cohorts. Roberts and Julian (86) observed that deaths

attributed to accidents and violence in the overall Inco Ontario nickel workers cohort yielded a statistically significant SMR of 1.39 (95% CI: 1.30-1.47). Shannon et al. (87) also observed a significant increase (SMR=1.61, 95% CI: 1.42-1.82) in accidents and violence mortality in the Sudbury Falconbridge cohort, primarily underground workers. The mining sector is known to have one of the highest rates of fatal accidents in North America (88). The regional mining analysis found slightly higher injury mortality across all accident categories in Elliot Lake miners, which is also consistent with the recognized higher rates of injury mortality in Northeastern Ontario than other regions of the province (89-91). Occupational injury mortality was a major concern in the early Elliot Lake uranium mining sub-cohort given the high rate of mine fatalities, suspected to be due to the quick rate of mine development and production prior to 1960, which ultimately prompted a provincial inquiry (92-94).

There are several strengths to the present update of the Ontario uranium miners cohort study including a large size and long period of follow-up, quality of exposure data, completeness of case ascertainment, and the national linkage. First, the broader inclusion criteria and use of multiple sources for enumeration allowed the creation of a large cohort with long follow-up that covered the entire period of exposures in Ontario uranium mining. The Ontario cohort continues to be one of the largest cohorts of uranium miners in the world, with high quality exposure assessment (25). The relatively low doses experienced by Ontario uranium miners compared to other cohorts of miners, allowed for detailed analyses of the risks associated with low dose radon exposure and provide a broad range that can apply to many different exposure scenarios. Also the large sample size allowed for an in depth analysis of many key factors that could modify the association between radon exposure and lung cancer risk.

A further strength of the present study is the use of two sources of exposure data, the MMF and the NDR. While previous updates of the cohort relied solely on the MMF, using the NDR increased the validity of the exposure assessment since the NDR has more complete data and extends the availability of exposure data past 1986 (end period for data available in the MMF). The NDR also provides some data on gamma radiation exposure, an important confounder for radon exposure and cancer risk. Appendix A describes the methods used to derive models to estimate individual gamma radiation estimates using this data.

This study allowed for the assessment of the potential impact of relying on exposure data from the MMF versus the NDR and suggests that the overall doses assigned to miners as well as the risk estimates derived were comparable when favoring one source of data over the other. However, there still remains other sources of uncertainty related to the exposure assessment and assignment that we were not able to measure directly. The six major sources of uncertainty that may affect the exposure ascertainment are presented in Schiager et al. (95) and Allodji et al.(96) and include natural variations in airborne radon gas concentrations, precision of measurement method, approximation of the Kusnetz conversion factor, systematic/human errors or operator in charge of air samples, estimation of working time, and lastly record-keeping and data transcription. A complete discussion of these sources of exposure uncertainty and the estimation of error for each source is provided in detail in Appendix B.

A major strength of the present study is its national mortality and cancer incidence linkages with the Generalized Iterative Record Linkage System (GIRLS) of Statistics Canada (72). Relative to other

systems worldwide linkage to the Canadian Mortality Database and Canadian Cancer Registry offers a near complete mortality and cancer incidence ascertainment. Case ascertainment from the Canadian provincial registries are said to be 90-95% complete by the North American Association of Central Cancer Registries (NAACR) (46).

The last major strength of this cohort is the national linkage for mortality and cancer incidence, which reduces loss to follow-up and allowed the identification of more incident cancers among miners who may have moved out of the province upon completing their employment. The national linkage for cancer incidence provides the first opportunity with this cohort to focus on the risk of cancer incidence, while previous updates of this cohort, as well as the majority of other international cohorts, have focused predominantly on lung cancer mortality. The size of this study also increased its ability to examine lung cancers by histology.

In the present cohort, we observed decreased overall mortality and cancer incidence external comparisons to the Canadian population. The most ready explanation is the healthy worker effect (97, 98). The healthy worker effect is liable to be more pronounced in this cohort due to the fact that over the early period of cohort employment to 1987 miners had to pass an annual physical and lung function test for certification for underground work (58, 63, 98). In addition, individual mining companies in Ontario often conducted their own physical examinations which were required for hire or continued employment and that from 1978 onward those with radon doses above the limit of 4 WLM annually or 2 WLM in a single quarter were removed from underground work (9, 10).

As in any cohort utilizing retrospective records and record linkage, there exists the possibility of ascertainment bias of workers who may have died or had an incident cancer diagnosed outside of Canada, though the thoroughness of the national record linkage should have mitigated that issue (55, 57, 76). The Canadian government began distributing social insurance numbers (SIN) to Canadians in 1965 and they are of use in cohort studies due to linkage with the Historical Summary Tax File (HSTF) used for vital status confirmation. Kusiak et al. observed a lung cancer SMR of 2.25 for the 63% of the cohort with social insurance numbers (SIN). Cohort members lacking a SIN number had a lung cancer SMR of 1.35 (14), indicating a large potential for underascertainment among this sub-group. Issues of poor ascertainment were somewhat mitigated in the present update by using a more conservative age cutoff for person years accumulation of 85 years and the inclusion of NDR uranium miner data with added identifiers may have increased reliability of the record linkage. Otherwise, reliability and thoroughness of vital ascertainment of linkage to the CMDB and HSTF have been well established with upwards of 98% of deaths and those alive at end of follow-up verified against alternate sources (73, 99, 100).

Despite the availability of exposure data from both the MMF and NDR there remains a possibility of non-differential misclassification in exposure due to potential unaccounted for or low precision estimates in early period radon doses (97). During the inception of uranium mining in Ontario up to 1967 RDP was measured with stationary area samples without a consistent schedule or extensive coverage throughout mines (9, 42). Due to this, doses attributed to workers had to be estimated by expert opinion and were thought to be subject to a fair degree of imprecision (42). From 1968 to 1980 samplers measured RDP in most areas of mines on a regular schedule that could be cross-

referenced with individual miner work schedules to estimate doses, which was subject to far less imprecision but were still not as precise as personal samplers (9, 42).

There are a number of potential co-exposures possible in the context of the Ontario uranium mining environment that could not be directly accounted for in the present study. These include crystalline silica, diesel exhaust, arsenic, and nickel. Analyses based on Ontario uranium mining regions with disparate levels of silica ore content and consequent exposures, however, did provide a crude method for assessing malignant and non-malignant respiratory disease risks in the cohort. The inability to account for these lung carcinogens warrants further investigation, as it may help to explain the peak in lung cancer mortality risk observed in the low cumulative radon exposure category (>0-1 WLM). Ultimately, the present study cannot directly address exposures aside from radon however the Occupational Cancer Research Centre (OCRC) at CCO is constructing a database of historic mining exposures in Ontario, which will be linked with MMF work history data in order to allow future exposure estimations, which can account for potential confounders and effect modifiers as documented in the present study.

What is known is that historically Ontario hard rock miners were known to be mobile with a range of mining experiences with different ores over their working lives (12). Multi-ore mining experience information was only available in the MMF and thus not for workers only found within NDR records. However, data on uranium mining experience outside of Ontario was present in both MMF and NDR records. Overall MMF database work histories (i.e., 93,500 miners) indicate that 52.1% of Ontario hard rock miners mined more than one type of ore, with 55.0% of the present cohort having mined other types of ore on top of uranium over the course of their work histories (12). Previous

cohort updates have concluded that the most significant ore mining other than uranium in terms of lung cancer development was gold mining, which was a major source of arsenic and silica exposure in Ontario (14, 59, 66). The typical pattern observed in past Ontario uranium cohort updates is that those with gold experience had higher subsequent lung cancer risks (14, 59). The findings from the present analysis are consistent in this regard, though as was noted by Muller et al. (59), those with gold mining experience were older than those without at the end of follow-up. Furthermore, the bulk of gold mining experience in the present cohort comes from those hired in the earliest period of study (i.e., 69.9% from 1954 – 1959), which were also known to be the dustiest periods characterized by rapid mine construction and production pre-1960 (refer to Figure 11) (41, 94). In an effort to further examine this period of high dust exposures, modern miners hired after 1970 were evaluated as a sub-cohort although risks among this group were comparable to the overall cohort.

An ever present concern with historical occupational mining cohorts, where lung cancer is the primary outcome is potential confounding and effect modification by smoking status of cohort members. Muller et al. (34, 59) found a possible multiplicative interaction between smoking and radon exposure in a case-control study of lung cancer cases in the Ontario cohort. Kusiak et al. (14) gathered and combined information from surveys and medical examinations dating from 1974 to 1991 in order to determine the smoking status of 4,971 cohort members. There was an 80% prevalence of cohort members having been regular cigarette smokers, which confirmed what Muller et al. (59) observed in their smaller case control study. Smoking prevalence was associated with birth cohorts such that the proportion of those who had not smoked cigarettes regularly increased by 2% for every 10 year increment in the year of birth beginning with the earliest survey of those born prior to 1938 having a 93% prevalence of regular smokers. However, there was no association

detected between the proportion of smokers and cumulative RDP exposure. Overall most uranium miner studies to date that have looked into the possible interaction between smoking status and radon exposure have found a relationship greater than additive but falling short of multiplicative (26-28, 59). Further underlying possible effect modification is the relation of smoking status and lung cancer histology. One of the largest lung cancer pooled datasets to date has established the prevalent histologic type for male smokers are Squamous cell carcinomas (SqCC), while Adenocarcinomas (AdCa) were more prevalent in never-smokers (101). It is worth noting that other diseases known to be related to tobacco use were not increased in comparison to the Canadian population, including circulatory diseases overall and in most circumstances non-malignant respiratory diseases excluding occupationally related pneumoconiosis.

In closing, this study was able to build on the understanding of health effects associated with radon exposure among uranium miners by performing an update of the Ontario uranium miners with 21 years of additional follow-up data. The large cohort and national linkage allowed this study to address several gaps in the literature including risks of cancer incidence, and associations with specific histological groups. However, some of the limitations of this study should be considered, such as the lack of smoking data, which could explain the differences seen in the histological group, as well as the lack of co-exposure data, which may explain some of the increased risks seen. Finally, the low doses experienced by these Ontario miners, particularly those employed after 1970, may be similar to the level of exposures experienced by present-day uranium miners provides valuable information to corroborate current radiation protection practices.

REFERENCES

1. Howe GR, Nair RC, Newcombe HB, Miller AB, Burch JD, Abbatt JD. Lung cancer mortality (1950-80) in relation to radon daughter exposure in a cohort of workers at the Eldorado Port Radium uranium mine: possible modification of risk by exposure rate. Journal of the National Cancer Institute. 1987;79(6):1255-60. eng.
2. Howe GR, Nair RC, Newcombe HB, Miller AB, Abbatt JD. Lung cancer mortality (1950-80) in relation to radon daughter exposure in a cohort of workers at the Eldorado Beaverlodge uranium mine. Journal of the National Cancer Institute. 1986;77(2):357-62. eng.
3. Chambers DB, Stager RH, Bernard FD, Lowe LM, editors. Reconstruction of the radon daughter exposure of Beaverlodge uranium workers. Eighth International Congress of the IRPA; 1992; Montreal.
4. Tilman A. On the Yellowcake Trail Part One: History of Uranium Mining in Canada. Watershed Sentinel. 2009:1.
5. Morrison HI, Villeneuve PJ, Lubin JH, Schaubel DE. Radon-progeny exposure and lung cancer risk in a cohort of Newfoundland fluorspar miners. Radiat Res. 1998;150(1):58-65. eng.
6. Villeneuve PJ, Morrison HI, Lane R. Radon and lung cancer risk: an extension of the mortality follow-up of the Newfoundland fluorspar cohort. Health Phys. 2007;92(2):157-69. eng.
7. Villeneuve PJ, Lane RSD, Morrison HI. Coronary heart disease mortality and radon exposure in the Newfoundland fluorspar miners' cohort, 1950-2001. Radiation and environmental biophysics. 2007;46(3):291-6. eng.
8. Villeneuve P, Morrison H. Radon Progeny Exposure and Lung Cancer: A Mortality Study of Newfoundland Fluorspar Miners 1950-2001. Technical. Ottawa, ON: Epistream Consulting Inc., 2005 RSP-0193.
9. Legislative Assembly of Ontario select committee on Ontario hydro affairs. Final report on the mining, milling and refining of uranium in Ontario. Toronto, ON 1980.
10. Runnalls OJC. Ontario's uranium mining industry: past, present, and future: a report prepared for the Ontario Ministry of Natural Resources. Toronto, Ontario, Canada: Ministry of Natural Resources; 1981.
11. Ham JM. Report of the Royal Commission on the Health and Safety of Workers in Mines. Toronto, ON: Ministry of the Attorney General, Province of Ontario; 1976.
12. Industrial Disease Standards Panel. Occupational disease issues about Lung Cancer in the Hardrock Mining Industry. Toronto, ON: Workers' Compensation Board of Ontario, Industrial Disease Standards Panel; 1994.
13. Do MT, Marrett LD, Purdha J, Lou W, Payne JI, Chon N. Ionising radiation exposure and risk of gastrointestinal cancers: a study of Ontario uranium miners. Occupational & Environmental Medicine. 2007;64(12):e34. eng.
14. Kusiak RA, Ritchie AC, Muller J, Springer J. Mortality from lung cancer in Ontario uranium miners. Br J Ind Med. 1993;50(10):920-8. eng.
15. Darby SC, Whitely E, Howe GR, Hutchings SJ, Kusiak RA, Lubin JH, et al. Radon and cancers other than lung cancer in underground miners: a collaborative analysis of 11 studies. Journal of the National Cancer Institute. 1995;87(5):378-84.

16. Lubin JH, Boice JD, Jr., Edling C, Hornung RW, Howe G, Kunz E, et al. Radon-exposed underground miners and inverse dose-rate (protraction enhancement) effects. Health Phys. 1995;69(4):494-500. eng.
17. Amabile J-C, Leuraud K, Vacquier B, Caër-Lorho S, Acker A, Laurier D. Multifactorial study of the risk of lung cancer among French uranium miners: radon, smoking and silicosis. Health Phys. 2009;97(6):613-21. eng.
18. Battista G, Belli S, Carboncini F, Comba P, Levante G, Sartorelli P, et al. Mortality among pyrite miners with low-level exposure to radon daughters. Scand J Work Environ Health. 1988;14(5):280-5. eng.
19. Roscoe RJ, Steenland K, Halperin WE, Beaumont JJ, Waxweiler RJ. Lung cancer mortality among nonsmoking uranium miners exposed to radon daughters. JAMA. 1989;262(5):629-33. eng.
20. National Research Council Committee on the Biological Effects of Ionizing R. Health Risks of Radon and Other Internally Deposited Alpha-Emitters: Beir IV. Washington (DC): National Academies Press (US); 1988. 602 p.
21. Bissett RJ, McLaughlin JR. Radon. Chronic Dis Can. 2010;29 Suppl 1:38-50. eng.
22. National Research Council. Health Effects of Exposure to Radon: BEIR Vol. VI. Washington: Joseph Henry Press [Imprint] National Academies Press; 1999. 516 p.
23. Chen X-A, Cheng Y-E, Rong Z. Recent results from a study of thorium lung burdens and health effects among miners in China. J Radiol Prot. 2005;25(4):451-60. eng.
24. Canadian Nuclear Safety Commission. Radon and health. Ottawa, ON: Canadian Nuclear Safety Commission; 2011. 16 p.
25. United Nations Scientific Committee on the Effects of Atomic Radiation. Effects of Ionizing Radiation: United Nations Scientific Committee on the Effects of Atomic Radiation-UNSCEAR 2006 Report to the General Assembly, with Scientific Annexes A and B. New York, N.Y.: United Nations Publications; 2009.
26. Finkelstein MM. Clinical measures, smoking, radon exposure, and risk of lung cancer in uranium miners. Occup Environ Med. 1996;53(10):697-702. eng.
27. L'Abbé KA. Lung cancer, radon daughter exposure, and smoking a nested case-control study within a cohort of uranium mine workers [Ph.D.]. Canada: University of Toronto (Canada); 1988.
28. Moolgavkar SH, Luebeck EG, Krewski D, Zielinski JM. Radon, Cigarette Smoke, and Lung Cancer: A Re-Analysis of the Colorado Plateau Uranium Miners' Data. Epidemiology. 1993;4(3):204-17. eng.
29. Stuart BO, Willard DH, Howard EB. Studies of inhaled radon daughters, uranium ore dust, diesel exhaust, and cigarette smoke in dogs and hamsters. Inhaled Part. 1970;1:543-60. eng.
30. Bijwaard H, Dekkers F, van Dillen T. Modelling lung cancer due to radon and smoking in WISMUT miners: preliminary results. Radiat Prot Dosimetry. 2011;143(2-4):380-3. eng.
31. Leuraud K, Schnelzer M, Tomasek L, Hunter N, Timarche M, Grosche B, et al. Radon, Smoking and Lung Cancer Risk: Results of a Joint Analysis of Three European Case-Control Studies Among Uranium Miners. Radiat Res. 2011;176(3):375-87. eng.
32. Lubin JH, Boice JD, Edling C, Hornung RW, Howe GR, Kunz E, et al. Lung Cancer in Radon-Exposed Miners and Estimation of Risk From Indoor Exposure. Journal of the National Cancer Institute. 1995;87(11):817-27. en.
33. Archer VE. Enhancement of lung cancer by cigarette smoking in uranium and other miners. Carcinog Compr Surv. 1985;8:23-37. eng.

34. Myers DK, Muller J, editors. Epidemiological follow-up of uranium miners in canada. Seventh International Congress of the International Radiation Protection Association; 1988. Sydney, Australia: Pergamon.
35. Tomasek L. Lung cancer risk from occupational and environmental radon and role of smoking in two Czech nested case-control studies. Int J Environ Res Public Health. 2013;10(3):963-79. eng.
36. Hunter N, Muirhead CR, Tomasek L, Kreuzer M, Laurier D, Leuraud K, et al. Joint analysis of three European nested case-control studies of lung cancer among radon exposed miners: exposure restricted to below 300 WLM. Health Phys. 2013 2013/03//;104(3):282-92.
37. Schnelzer M, Hammer GP, Kreuzer M, Tschense A, Grosche B. Accounting for smoking in the radon-related lung cancer risk among German uranium miners: results of a nested case-control study. Health Phys. 2010 2010/01//;98(1):20-8.
38. National Research Council. Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2. The National Academies Press, 2006 9780309091565.
39. Lubin JH, Tomásek L, Edling C, Hornung RW, Howe G, Kunz E, et al. Estimating lung cancer mortality from residential radon using data for low exposures of miners. Radiat Res. 1997;147(2):126-34. eng.
40. United Nations Scientific Committee on the Effects of Atomic Radiation. Effects of Ionizing Radiation: United Nations Scientific Committee on the Effects of Atomic Radiation-UNSCEAR 2006 Report to the General Assembly, with Scientific Annexes C, D, and E. New York, N.Y.: United Nations Publications; 2009. 334 p.
41. Dsma Atcon, Atomic Energy Control Board of Canada. Elliot Lake Study - Factors Affecting the Uranium Mine Working Environment Prior to the Introduction of Current Ventilation Practices. Technical. Ottawa, Ontario: Atomic Energy Control Board of Canada, 1985 INFO-0154.
42. Shannon H. Report to the Workers' Compensation Board on the Ontario uranium mining industry. Toronto: Industrial Disease Standards Panel; 1989.
43. Robinson I. The costs of uncertainty: regulating health and safety in the Canadian uranium industry. Technical. Kingston, ON, Canada: Queen's University, Centre for Resource Studies, 1982 24.
44. Schubauer-Berigan MK, Daniels RD, Pinkerton LE. Radon exposure and mortality among white and American Indian uranium miners: an update of the Colorado Plateau cohort. Am J Epidemiol. 2009 Mar 15;169(6):718-30. PubMed PMID: 19208723. Epub 2009/02/12. eng.
45. Boice JD, Jr., Cohen SS, Mumma MT, Chadda B, Blot WJ. A cohort study of uranium millers and miners of Grants, New Mexico, 1979-2005. J Radiol Prot. 2008 Sep;28(3):303-25. PubMed PMID: 18714128. Epub 2008/08/21. eng.
46. Lane RSD, Frost SE, Howe GR, Zablotska LB. Mortality (1950-1999) and cancer incidence (1969-1999) in the cohort of Eldorado uranium workers. Radiat Res. 2010;174(6):773-85. eng.
47. Zablotska LB, Lane RSD, Frost SE, Thompson PA. Leukemia, lymphoma and multiple myeloma mortality (1950-1999) and incidence (1969-1999) in the Eldorado uranium workers cohort. Environ Res. 2014;130:43-50. eng.
48. Tomasek L. Lung cancer mortality among Czech uranium miners-60 years since exposure. Journal of radiological protection. 2012;32(3):301-14. PubMed PMID: 22809823. eng.
49. Tomasek L. Effect of age at exposure in 11 underground miners studies. Radiation protection dosimetry. 2014 2014/04/20/;160:124-7.

50. Rage E, Caer-Lorho S, Drubay D, Ancelet S, Laroche P, Laurier D. Mortality analyses in the updated French cohort of uranium miners (1946-2007). International archives of occupational and environmental health. 2014 Nov 20. PubMed PMID: 25410273. Epub 2014/11/21. Eng.
51. Sogl M, Taeger D, Pallapies D, Brüning T, Dufey F, Schnelzer M, et al. Quantitative relationship between silica exposure and lung cancer mortality in German uranium miners, 1946-2003. Br J Cancer. 2012;107(7):1188-94. eng.
52. Walsh L, Grosche B, Schnelzer M, Tschense A, Sogl M, Kreuzer M. A REVIEW OF THE RESULTS FROM THE GERMAN WISMUT URANIUM MINERS COHORT. Radiat Prot Dosimetry. 2014 Sep 28. PubMed PMID: 25267854. Epub 2014/10/01. Eng.
53. Kreuzer M, Dufey F, Marsh JW, Nowak D, Schnelzer M, Walsh L. Mortality from cancers of the extra-thoracic airways in relation to radon progeny in the Wismut cohort, 1946-2008. Int J Radiat Biol. 2014 2014/11//;90(11):1030-5.
54. Kreuzer M, Dufey F, Sogl M, Schnelzer M, Walsh L. External gamma radiation and mortality from cardiovascular diseases in the German WISMUT uranium miners cohort study, 1946-2008. Radiation and environmental biophysics. 2013 2013/03//;52(1):37-46.
55. Woodward A, Roder D, McMichael AJ, Crouch P, Mylvaganam A. Radon daughter exposures at the Radium Hill uranium mine and lung cancer rates among former workers, 1952-87. Cancer Causes Control. 1991 Jul;2(4):213-20. PubMed PMID: 1873450. Epub 1991/07/01. eng.
56. Lubin JH, Liang Z, Hrubec Z, Pershagen G, Schoenberg JB, Blot WJ, et al. Radon exposure in residences and lung cancer among women: combined analysis of three studies. Cancer Causes Control. 1994;5(2):114-28. eng.
57. Muller J, Wheeler WC. Causes of death in Ontario uranium miners. Occupational Safety and Health. 1974;32(29):29-42. eng.
58. Muller J, Wheeler WC, Gentleman JF, Suranyi G, Kusiak RA, editors. Study of Mortality of Ontario miners. International conference on Occupational Radiation Safety in Mining; 1985. Toronto, ON: Canadian Nuclear Association.
59. Muller J, Kusiak RA, Ritchie AC. Factors modifying lung cancer risk in Ontario uranium miners, 1955-1981. Toronto, ON: Ontario Ministry of Labour; Ontario Workers' Compensation Board; Atomic Energy Control Board of Canada, 1989.
60. Hornung RW. Health effects in underground uranium miners. Occup Med. 2001;16(2):331-44. eng.
61. Muir DC, Shannon HS, Julian JA, Verma DK, Sebestyen A, Bernholz CD. Silica exposure and silicosis among Ontario hardrock miners: I. Methodology. Am J Ind Med. 1989;16(1):5-11. eng.
62. Do MT. Ionizing Radiation Exposure and Risk of Gastrointestinal Cancer: A Study of the Ontario Uranium Miners [Ph.D.]. Toronto, ON: The University of Toronto; 2009.
63. Muller J, Wheeler WC, Gentleman JF, Suranyi G, Kusiak RA. Study of mortality of Ontario miners 1955-1977, Part I. Toronto and Ottawa: Ontario, Ministry of Labour; Ontario Workers' Compensation Board; Atomic Energy Control Board of Canada, 1983.
64. Ashmore JP, Grogan D. The National Dose Registry for Radiation Workers in Canada. Radiation Protection Dosimetry. 1985;11(2):95-100.
65. Kusiak RA, Ritchie AC, Springer J, Muller J. Mortality from stomach cancer in Ontario miners. Br J Ind Med. 1993;50(2):117-26. eng.

66. Kusiak RA, Springer J, Ritchie AC, Muller J. Carcinoma of the lung in Ontario gold miners: possible aetiological factors. Br J Ind Med. 1991;48(12):808-17. eng.
67. Sont W, Ashmore JP. 1998 report on occupational radiation exposures in Canada. Technical. Ottawa, Ontario, Canada: Health Canada, Environmental Health Directorate, Radiation Protection Branch, 1998 1998. Report No.: H46-2/98-223E.
68. Ashmore JP, Krewski D, Zielinski JM, Jiang H, Semenciw R, Band PR. First analysis of mortality and occupational radiation exposure based on the National Dose Registry of Canada. Am J Epidemiol. 1998 1998/09/15/;148(6):564-74. eng.
69. Sont WN, Zielinski JM, Ashmore JP, Jiang H, Krewski D, Fair ME, et al. First analysis of cancer incidence and occupational radiation exposure based on the National Dose Registry of Canada. Am J Epidemiol. 2001 2001/02/15/;153(4):309-18. eng.
70. Ashmore JP, Gentner NE, Osborne RV. Incomplete data on the Canadian cohort may have affected the results of the study by the International Agency for Research on Cancer on the radiogenic cancer risk among nuclear industry workers in 15 countries. Journal of radiological protection: official journal of the Society for Radiological Protection. 2010 2010/06//;30(2):121-9. eng.
71. Zielinski JM, Shilnikova NS, Krewski D. Canadian National Dose Registry of radiation workers: overview of research from 1951 through 2007. Int J Occup Med Environ Health. 2008 2008;21(4):269-75. eng.
72. Fair M. Generalized record linkage system: Statistics Canada's record linkage software. Austrian Journal of Statistics. 2004;33(1&2):37-53.
73. Goldberg MS, Carpenter M, Thériault G, Fair M. The accuracy of ascertaining vital status in a historical cohort study of synthetic textiles workers using computerized record linkage to the Canadian Mortality Data Base. Can J Public Health. 1993;84(3):201-4. eng.
74. Breslow NE, Day NE. Statistical methods in cancer research volume II - The design and analysis of cohort studies. Lyon, France: International Agency for Research on Cancer; 1987. 406 p.
75. Checkoway H, Pearce NE, Kriebel D. Research Methods in Occupational Epidemiology: Oxford University Press; 2004. 404 p.
76. Pearce N, Checkoway H, Dement J. Exponential models for analyses of time-related factors, illustrated with asbestos textile worker mortality data. Journal of occupational medicine : official publication of the Industrial Medical Association. 1988 Jun;30(6):517-22. PubMed PMID: 3392615. Epub 1988/06/01. eng.
77. Lubin JB, JDJ; Edling, C; Hornung, RW; Howe, GR; Kunz, E; Kusiak, RA; Morrison, HI; Radford, EP; Samet, JM et al. Radon and lung cancer risk: a joint analysis of 11 underground miners studies. US Dept. of Health and Human Services, Public Health Service, National Institutes of Health, 1994 Contract No.: 94.
78. Rothman KJ. Induction and latent periods. Am J Epidemiol. 1981;114(2):253-9. eng.
79. Forman D, International Agency for Research on C, International Association of Cancer R. Cancer incidence in five continents, Volume X. Lyon; Geneva: International Agency for Research on Cancer ; Distributed by WHO Press, World Health Organization; 2013.
80. Brenner DJ. The significance of dose rate in assessing the hazards of domestic radon exposure. Health Phys. 1994 Jul;67(1):76-9. eng.
81. Kreuzer M, Muller KM, Brachner A, Gerken M, Grosche B, Wiethege T, et al. Histopathologic findings of lung carcinoma in German uranium miners. Cancer. 2000;89(12):2613-21. PubMed PMID: 11135223. eng.

82. Wu-Williams AH, Samet JM. Lung cancer and cigarette smoking. In: Samet JM, editor. Epidemiology of lung cancer. New York: Marcel Dekker, Inc.; 1994.
83. Patterson JF. Silicosis in Hardrock Miners in Ontario. Toronto, ON: Ontario Department of Mines, Mines ODo; 1959 158.
84. Patterson JF. Silicosis in Hardrock Miners in Ontario (A Further Study). Toronto, ON: Ontario Department of Mines, Mines ODo; 1973 173.
85. Verma DK, Rajhans GS, Malik OP, des Tombe K. Respirable dust and respirable silica exposure in Ontario gold mines. J Occup Environ Hyg. 2014;11(2):111-6. eng.
86. Roberts RS, Julian JA, Sweezey D, Muir DC, Shannon HS, Mastromatteo E. A study of mortality in workers engaged in the mining, smelting, and refining of nickel. I: Methodology and mortality by major cause groups. Toxicol Ind Health. 1989;5(6):957-74. eng.
87. Shannon HS, Walsh C, Jadon N, Julian JA, Weglo JK, Thornhill PG, et al. Mortality of 11,500 nickel workers--extended follow up and relationship to environmental conditions. Toxicol Ind Health. 1991;7(4):277-94. eng.
88. Groves WA, Kecojevic VJ, Komljenovic D. Analysis of fatalities and injuries involving mining equipment. Journal of Safety Research. 2007 2007/01//;38(4):461-70.
89. Bains N, Dall K, Hay C, Pacey MA, Sarkella J, Ward M. Population Health Profile--North East LHIN. Government. Toronto, ON: Ontario Ministry of Health and Long-Term Care, 2006.
90. Lightfoot N, Berriault C, Semenciw R. Mortality and cancer incidence in a nickel cohort. Occup Med (Lond). 2010;60(3):211-8. eng.
91. Rowe BH, Therrien S, Johnson C, Sahai VS, Bota GW. Regional variations of northern health: the epidemic of fatal trauma in northeastern Ontario. Can J Public Health. 1995;86(4):249-54. eng.
92. MacDowell LS. The Elliot Lake Uranium Miners' Battle to Gain Occupational Health and Safety Improvements, 1950–1980. Labour/Le Travail. 2012;69(1):91-118.
93. Morrison RGK. Report of the Special Committee on Mining Practices at Elliot Lake - Part 1. Accidents and Related Representations. Government. Toronto: Ontario Department of Mines, 1959 155-1.
94. Morrison RGK. Report of the Special Committee on Mining Practices at Elliot Lake - Part 2. Accident Review, Ventilation, Ground Control, and Related Subjects. Government. Toronto: Ontario Department of Mines, 1961 155-2.
95. Schiager KJ BT, Johnson JA. Radiation monitoring for uranium miners: evaluation and optimization. *ALARA Inc. Final Report on Contract No. J0295026*, 1981.
96. Allodji RS, Leuraud K, Bernhard S, Henry S, Benichou J, Laurier D. Assessment of uncertainty associated with measuring exposure to radon and decay products in the French uranium miners cohort. J Radiol Prot. 2012 Mar;32(1):85-100. PubMed PMID: 22392893. Epub 2012/03/07. eng.
97. Pearce N, Checkoway H, Kriebel D. Bias in occupational epidemiology studies. Occup Environ Med. 2007;64(8):562-8. eng.
98. Howe GR, Chiarelli AM, Lindsay JP. Components and modifiers of the healthy worker effect: evidence from three occupational cohorts and implications for industrial compensation. Am J Epidemiol. 1988;128(6):1364-75. eng.
99. Schnatter AR, Acquavella JF, Thompson FS, Donaleski D, Thériault G. An analysis of death ascertainment and follow-up through statistics Canada's Mortality Data Base system. Can J Public Health. 1990;81(1):60-5. eng.

100. Krewski D, Dewanji A, Wang Y, Bartlett S, Zielinski JM, Mallick R. The effect of record linkage errors on risk estimates in cohort mortality studies. Survey Methodology. 2005;31(1):13-21. eng.
101. Pesch B, Kendzia B, Gustavsson P, Jöckel K-H, Johnen G, Pohlabeln H, et al. Cigarette smoking and lung cancer--relative risk estimates for the major histological types from a pooled analysis of case-control studies. Int J Cancer. 2012;131(5):1210-9. eng.

APPENDIX A:

Exploratory Analyses of Potential Health Risks Associated with Gamma Radiation Exposure among Ontario Uranium Miners

Background

The International Agency for Research on Cancer (IARC) considers gamma radiation as a Group 1 carcinogen based an evaluation of extensive evidence from both animal and human data. IARC concluded that there is "*sufficient evidence*" that gamma radiation is carcinogenic to humans [1]. Compared to other occupations, on average, uranium miners are exposed to much higher levels of gamma radiation than any other occupations, including those working in the medical, research, and nuclear industry [1, 2]. This is not surprising given that underground uranium miners worked within completely enclosed uranium ore bodies that emit gamma energy from all directions. Because of the harsh working conditions, these miners did not wear the necessary protective equipment (e.g., lead apron) that would shield them against gamma radiation. Despite the high risk of developing cancer due to direct exposure to high levels of gamma radiation, there is little research being conducted to assess cancer risks among these miners. In part, gamma exposure data are not available to conduct epidemiological assessment of potential adverse health effects. In fact, in Canada, no data on gamma radiation exposure was systematically collected until 1981, almost 25 years after the first uranium mine opened in Ontario.

As Duport [3] and Utting [4, 5] have pointed out, historically, the risk of lung cancer in uranium mines has been attributed to inhaled radon daughters (^{222}Rn) alone because doses from other sources of radiation were considered to be insignificant [3] or their effects would have been automatically included in epidemiological studies [4, 5]. This rationale has been challenged over recent years citing that radon levels have progressively reduced in modern mining due to better ventilation practices. However, gamma radiation is unaffected by ventilation practices and as such would have remained constant [4, 5]. Furthermore, since gamma radiation are energy waves unlike radon alpha particles, it

can penetrate deep inner tissues that would otherwise be un-impacted by radon daughters alone [6]. In fact, risks of leukemia from acute and high doses of gamma radiation are well-characterized, but risks from lower doses and dose-rates are not well established, particularly for underground uranium miners.

Concerns over the need to monitor miners for gamma radiation exposure started in the mid-1970s with a pilot study conducted in 1977 to investigate the gamma radiation exposure in three Ontario mines [4, 5]. The results of this study provided evidence that the gamma dose for a few employees had actually exceeded the maximum permissible annual dose [4, 5]. Utting also found that whole body dose due to exposure to gamma radiation can reach 30 mSv per year and higher in underground mines where the average uranium ore grade is 0.1 percent [5].

Although uranium production in Ontario Canada began in the mid-1950s, monitoring of uranium miners for gamma radiation exposure was only initiated in 1981 by the National Dose Registry. Given that most uranium miners were employed prior to this period, associated health risks for these miners could not be evaluated. As such, a method is needed to estimate historical exposure to gamma radiation in order to explore potential associated health risks if any. The exploratory work presented in the Appendix represents initial efforts in addressing this knowledge gap.

Objectives

This exploratory work has two objectives and these are as follows:

1. To develop a statistical method for estimating historical exposures to gamma radiation prior to 1981;
2. Conduct preliminary risk estimates of potential associated health risks.

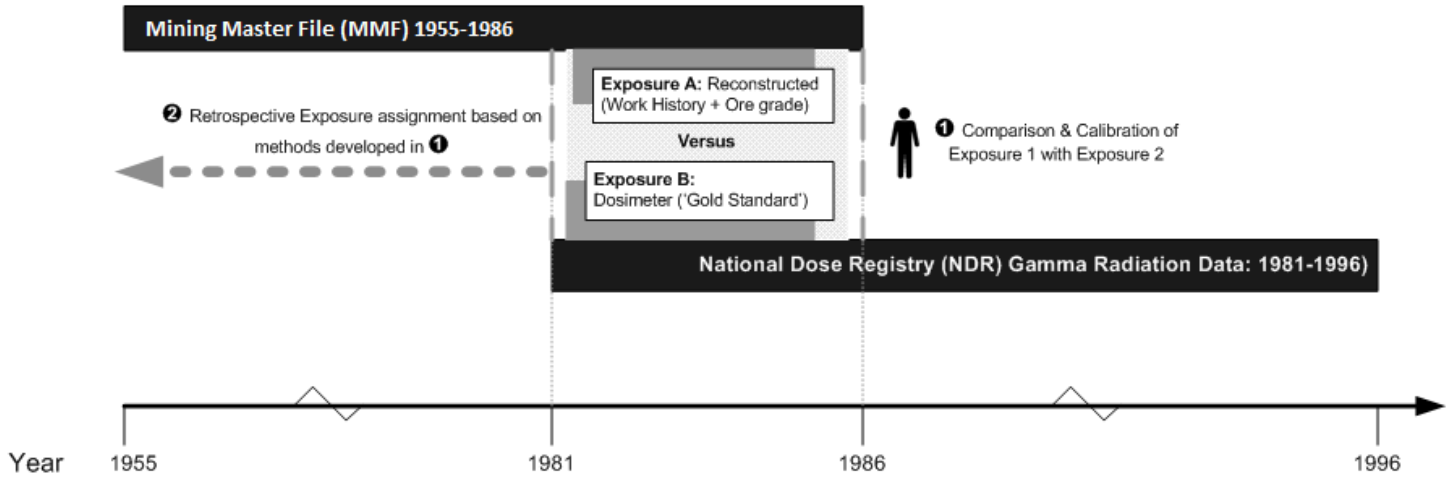
Methods

The analyses conducted in this exploratory study are based only on workers employed at Denison Mines. It is the largest mine, employed the most number of workers and operated between 1954 and 1992. Workers from other mines were not included since mine parameters (e.g., ore grade) are not currently available or the sample sizes are insufficent for reliable estimates.

Overview of Approach Used for Estimation of Missing Gamma Doses

Beginning in 1981, the National Dose Registry began systematic collection of dosimetric information on gamma radiation exposure for Ontario uranium underground miners. At the same time, the Mining Master File (MMF) started to phase out and was discontinued completely by 1986. As shown in Figure 1, estimation of gamma dose based on the period between 1981 and 1986. During this period, the work history information available from the MMF was used to calibrate measured dosimetric gamma radiation from the National Dose Registry (NDR dose). Mine characteristics (e.g, ore milled, ore grade, and other geological parameters collated annually) collated through manual extraction of historical mining information on paper records were also used to increase precision of the predictive modeling of gamma dose.

Figure 1: Overview of approach of gamma dose estimation approach.



Statistical Approach of Estimating Historical Gamma Doses

The unit of analysis was employment records. Initial descriptive statistics were conducted to examine the distribution of the data points. The need to transform continuous variables was examined by normal probability plots. Since the exposure variable (e.g., radon in Working Level Months and NDR gamma dosimetric readings) was positively skewed, a log transformation was taken.

In order to validate the prediction procedures that were developed, random split-samples of the employment records were used; "Training Sample" representing 70 percent of employment records, and "Test Sample" representing 30 percent of employment records. This included first the development of dose prediction models followed by the determination of model performance based on predictability of gamma dose.

The dose prediction models were constructed using traditional (standard) and recently available robust multiple linear regression methods in SAS version 9.1. A stepwise approach was used to select variables into the model. Criteria for retaining the variables in the model was based on a p-value of ≤0.15. Model fit was assessed using adjusted R-square. Co-linearity was determined by the magnitude of the variance inflation factor (VIF). Variables with VIF greater than 3.0 were removed from the model. All doses were estimated blinded from cases status.

Health Risks Associated with Exposures to Gamma Radiation

For statistical methods for estimating associated health risks (i.e., risk estimates), please refer to Section 4.1.2 of the main report for description of internal cohort analysis. All gamma doses estimated for this exploratory analysis were conducted blinded from case status.

Results/Discussions

Gamma Dose Estimation

The external radiation doses were not available for Ontario uranium miners who worked prior to 1981. Therefore, before proceeding with assessing health risks, a method was needed to estimate historical exposures. In this exploratory analysis, dose prediction models were developed and validated using a split sample cross-validation approach. Independent parameters such as work history and mine characteristics were regressed against the NDR measured doses (NDR dose) using a multiple linear regression. Examples of mine characteristics included in the model was uranium ore grade (Figure 1a) which is highly correlated to gamma dose rate (R^2=0.97, Figure 1b). It was also observed that mining characteristics alone are inadequate in assigning exposure to individual miners. As such, work history (e.g., months worked) was also included in the model to estimate gamma doses. Overall, the correlation between the estimated (modeled) doses and NDR measured doses were reasonable but not perfect (r=0.401, p<0.01). Figure 3 shows the mean gamma doses by calendar year. As expected, there were some differences between modeled doses and measured doses (NDR dose). On average, modeled doses (Mean = 1.81, SD 0.3) are lower than measured doses (Mean = 3.8, SD 3.1). The differences could, in part, be explained by the variability

in the NDR doses where there are dosimetry badges of workers who were exposed to 30 mSv in a given year. These could be either true doses or simply the result of badges forgotten in mines when the worker was no longer working. Conversely, the estimated doses obtained from predicted models were less likely to be influenced by extreme values due to the nature of the Proc Reg Robust procedure in SAS where less weight was given to extreme values. Similarly, there are many instances where miners had identical work histories but had remarkably different NDR doses. Therefore, it is important to further investigate additional sources of uncertainties.

Health Risk Assessment

As part of the exploratory analyses, potential health risks were assessed for exposures to gamma radiation from uranium mining. As shown in Table 1, the estimates were derived for workers employed at Denison Mines. In total, there were 12,953 miners contributing 431,655 person-years of observation. Tables 2 to 4 show the results of the preliminary risk estimates for cardiovascular diseases, and leukemia mortality.

For the study period, there were 494 lung cancer deaths from miners employed at Denison Mines. Risk estimates were derived for 0 and 10 year lags in exposure to take into account latency of disease diagnosis. Overall, no statistically significant increases in lung cancer risks with increasing gamma exposure were observed (Table 2). Using a 10-year exposure lag, miners with a cumulative gamma dose greater than 10 mSv had an 11% increase in lung cancer mortality risk, however, the increase was not statistically significant ($p>0.05$).

For cardiovascular diseases, there were 992 deaths from miners employed at Denison Mines. Risk estimates were derived for 0 and 5 year lags in exposure to take into account latency of disease diagnosis. Overall, no statistically significant increases were observed with no evidence of a dose-response relationship (Table 3).

For the study period, there were 28 leukemia deaths from miners employed at Denison Mines. Given hematopoietic malignancies have a short latency period, risk estimates were derived for 0 and 2 year lags in exposure. Given the small number of cases, only 3 exposure data categories were constructed (Table 4). For the 'No Lag' analysis, there were no statistically significant association observed, but an increased risk was observed in the highest cumulative dose category suggesting a dose-response relationship. When the exposures were lagged by two years, a significant risk was observed for the highest cumulative dose (>14 mSv) category. When compared to the referent group there was a significant dose-response increase (RR=2.58, 95%CI 1.06-6.3). This finding was rather surprising given the low dose and therefore, it is possible that the result was confounded by other factors. However, we do not have additional data to test potential competing hypotheses. For example, the impact of smoking could be contributing to the observed results but we do not have smoking information to adjust for this risk factor. Smoking is a weak risk factor for hematopoietic malignancies, though smoking was highly prevalent among these workers [7]. Non-smokers would have also been exposed to tobacco smoke through second-hand exposure. As such, it is unlikely that potential confounding factors such as smoking would have a significant impact on leukemia mortality in this cohort. While this result is unexpected, it is not the first study to identify an association. Rericha and colleagues also observed increased risk for all leukemias combined (RR =

1.63; 95% CI, 1.05–2.54; p = 0.03) and CLL (RR = 1.96; 95% CI, 1.12–3.42; p = 0.02) when comparing exposures in the 80th percentile (20 mGy) to the 20th percentile (1 mGy) [8]. Further research is necessary to further understand the risks of hematologic cancers from low-dose exposures to gamma radiation.

Summary

The results presented herein are exploratory in nature and as such are considered to be preliminary. Like any modeling, there are many sources of uncertainties. As a result of this exploratory work, we have identified other opportunities to enhance the precision of historical dose estimates. For example, through this work, we have compiled new information available only in paper records of work history, mine geology, and mine practices that could further improve the dose reconstruction and to expand beyond Denison Mines and other mines operated in Ontario. This work could further support research necessary for better understanding of the risks of hematologic cancers from low-dose exposures to gamma radiation.

References

1. International Agency for Research on Cancer, Monographs on the Evaluation of Carcinogenic Risk to Humans: Ionizing Radiation, Part 1: X- and Gamma (g)-Radiation, and Neutrons. 1988, International Agency for Research on Cancer: Lyon. p. Vol 75.
2. United Nations Scientific Committee on the Effects of Atomic Radiation, Ionizing Radiation: Sources and Biological effects, Annex D. 1993.
3. Duport, P., Is the radon risk overestimated? Neglected doses in the estimation of the risk of lung cancer in uranium underground miners. Radiat Prot Dosimetry, 2002. 98(3): p. 329-38.
4. Utting R.E., An Assessment of Gamma Exposure of Miners in Three Ontario Uranium Mines. 1978, Atomic Energy Control Board (AECB-1172).
5. Utting R.E., Assessment of Gamma Doses Absorbed By Underground Miners In Canadian Uranium Mines, in Radiation Hazards In Mining: Control, Measurement, And Medical Aspects. 1981. p. Chapter 81, p.533-538.
6. Agency for Toxic Substances and Disease Registry, Toxicological Profile for Ionizing Radiation. 1999, US Department of Human Health and Services: Atlanta, Georgia. p. 41.
7. Kusiak RA, Ritchie AC, Muller J, Springer J. Mortality from lung cancer in Ontario uranium miners. Br J Ind Med. 1993;50(10): 920-928.
8. Řeřicha, V., Kulich M., Řeřicha R, Shore D. L., and Sandler D. P. Incidence of Leukemia, Lymphoma, and Multiple Myeloma in Czech Uranium Miners: A Case–Cohort Study. Environ Health Perspect. 2006 Jun; 114(6): 818–822.

Exploratory Analysis 1: Gamma Dose Estimation

Figure 2: Uranium Ore grade from Denison Mines (1957-1986).

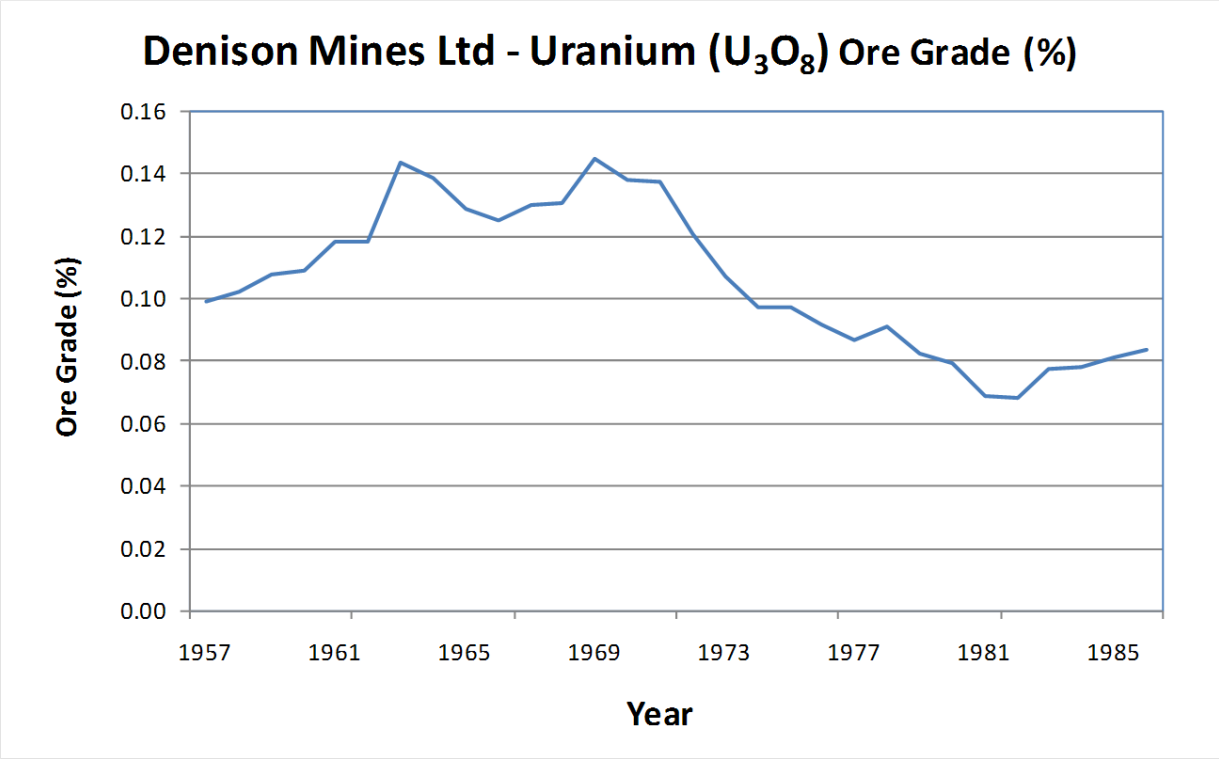


Figure 3: Relationship between dose rate (mRh^{-1}) and ore grade for Denison Mines (1957-1986)

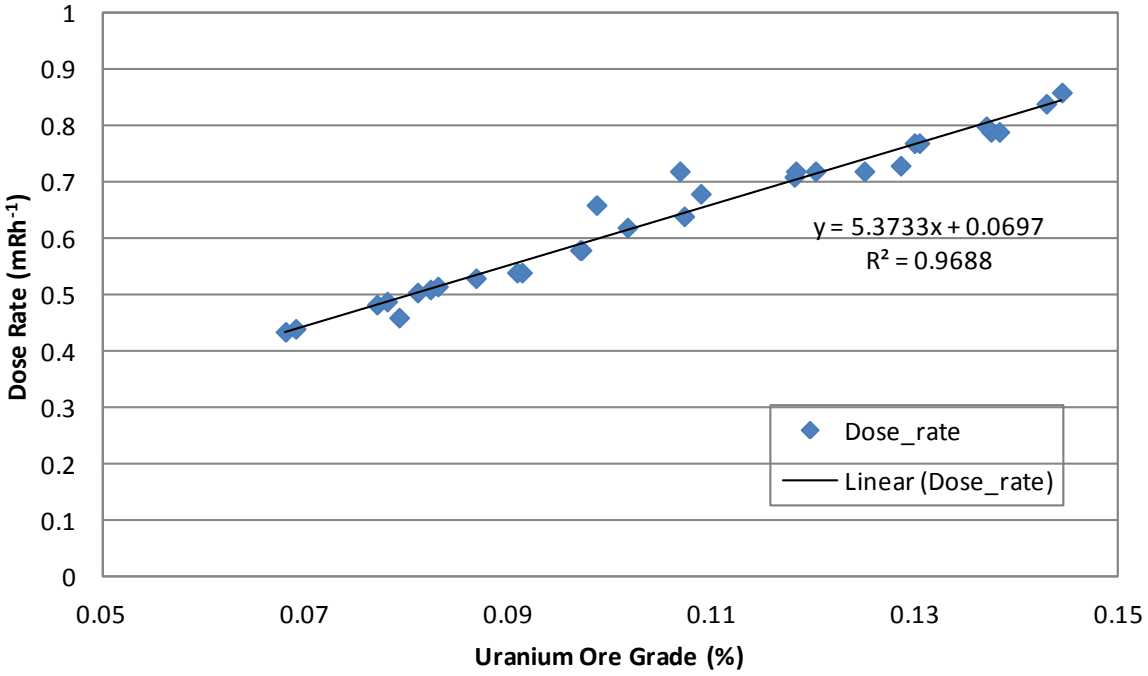
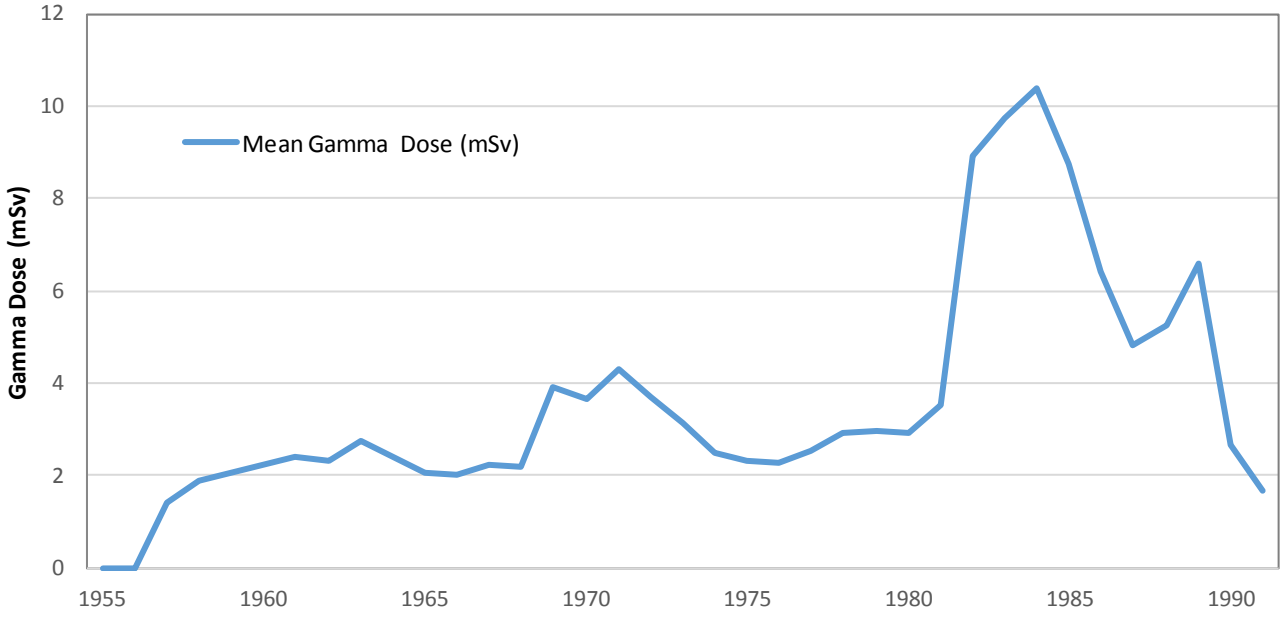


Figure 4: Estimated average annual gamma doses (mSv) by calendar years for Denison Mine workers



Exploratory Analysis 2: Health Risk Assessment

Table 1: Cohort of workers employed at Denison Mines in Ontario Canada

Characteristics of cohort	Characteristics
Cohort Size	12,953
Person years of follow-up (mortality)	431,655
Age (years) at first Employment [n (%)]	
<22 years	3,248 (25)
22 - <27	3,630 (28)
27 - <34	3,145 (24)
34+	2,930 (23)
Mean (SD)	28 (8.4)

Table 2: Lung cancer mortality by cumulative exposure to gamma radiation among Denison Uranium miners

Exposure Lag	Cumulative Gamma Dose (mSv)	Person Years	Cases	RR (95%CI)
No Lag	0-1.5	111,554	94	1.00 (Referent)
	>1.5-3.5	102,150	139	1.00 (0.77-1.3)
	>3.5-10	113,028	134	0.81 (0.62-1.06)
	>10	104,923	127	1.02 (0.78-1.33)
10 Year Lag	0-1.5	206,418	104	1.00 (Referent)
	>1.5-3.5	74,625	137	1.08 (0.08-1.14)
	>3.5-10	82,249	136	0.91 (0.7-1.18)
	>10	68,363	117	1.11 (0.85-1.45)

Notes: Adjusted for attained age, period

Table 3: Cardiovascular Disease mortality by cumulative exposure to gamma radiation among Denison Uranium miners

Exposure Lag	Cumulative Gamma Dose (mSv)	Person Years	Cases	RR* (95%CI)
No Lag	0-1.5	111,554	92	1.00 (Referent)
	>1.5-3.5	102,150	254	0.93 (0.77-1.13)
	>3.5-10	113,028	304	0.95 (0.79-1.14)
	>10	104,923	242	0.98 (0.81-1.19)
5 Year Lag	0-1.5	159,319	208	1.00 (Referent)
	>1.5-3.5	88,317	252	0.95 (0.79-1.15)
	>3.5-10	97,508	298	0.96 (0.8-1.15)
	>10	86,512	234	1.01 (0.84-1.22)

Notes: *Adjusted for attained age, period

Table 3: Leukemia mortality by cumulative exposure to gamma radiation among Denison Uranium miners

Exposure Lag	Cumulative Gamma Dose (mSv)	Person Years	Cases	RR* (95%CI)
No Lag	0 - 4	238,606	11	1.00 (Referent)
	>4.0 - 14	110,748	8	1.39 (0.56-3.47)
	>14	82,302	9	2.43 (1.00-5.92)
2 Year Lag	0 - 4	251,013	11	1.00 (Referent)
	>4.0 - 14	104,375	8	1.46 (0.59-3.64)
	>14	76,267	9	2.58 (1.06-6.3)

Notes: *Adjusted for attained age, period

APPENDIX B: Sources of Exposure Uncertainty

High quality exposure data is crucial for the accurate assessment of risks experienced by uranium miners from exposure to radon. Traditionally, Ontario has been regarded to have some of the best exposure data on underground uranium miners (1). As with any exposure data, however, there are certain assumptions and inherent errors that may affect accurate exposure assessment. This section aims to discuss and estimate the percentage of error associated with some of the key sources of exposure uncertainty, as a preliminary step to assessing the effects that exposure uncertainty may have on the risk estimates.

The six major sources of exposure uncertainty examined in this study were taken from Schiager et al. (2) and Allodji et al.(3) and include natural variations in airborne radon gas concentrations, precision of measurement method (Kusnetz method), approximation of the Kusnetz conversion factor, systematic/human errors including operator in charge of air samples, estimation of working time, and lastly record-keeping and data transcription. The magnitude of uncertainty related to each source are discussed below in detail and summarized in Table 1. The periods of interest chosen in Table 1 were based on the information presented in the Methods section, radon exposure assessment subsection, which outlines the periods in Ontario mines with the most notable changes in exposure assessment. Due to the high degree of uncertainty in the earliest period of exposure (1954-1957), where exposure estimates were predominately extrapolated by mine engineers, this period was excluded from this analysis. However, since there were few miners employed during this period and this period represents a small percentage of the total period of exposure so it would not have a significant influence on miners true cumulative exposure.

Table 1. Sources and magnitude of uncertainty associated with estimating exposure to radon

Sources	Periods	
	1958-1967	1968-1996
Natural Variations in Radon Concentrations	52-62%	30-36%
Estimation of Working Time	8%	4%
Precision of the Kusnetz Method	3-23%	0.3-2.3%
Kusnetz time factor	3.5%	3.5%
Systematic Errors Human Error-Operator in charge of taking air samples	5-10% 2-3%	5-10% 2-3%
Record Keeping and Data Transcription	1.5%	1.5%
Total uncertainty	53.1-67.5%	30.9-37.8%

Natural Variations in Radon Concentrations

The largest contribution to the uncertainty of radon exposure measurements in the mines comes from natural fluctuations in the mine over time. According to Schiager et al. the concentration of radon progeny in the mine is influenced by the type of mining operation, ore grade and most importantly by the amount of ventilation (2). As seen in an exposure reconstruction study of Beaverlodge uranium workers, there is much variability in individual work area concentrations of radon, which, according to the study means exposure estimates derived using mine wide averages may be dramatically under or over estimating an individual miners true exposure to radon (4). As reported by Schiager et al., two Canadian studies have performed detailed statistical analyses on ambient measurements taken in several mines over several days. These studies found that the measurements varied dramatically from 5 to 95% (5) and 21-74% (6) for individual mine locations with an average variation across all locations of 30% and 36% (2). This indicates a roughly 30-36% variation in radon concentrations

between routine sampling. This value applies to the 1968 period when ambient sampling occurred more systematically. However, for the period 1958-1967 samples were less systematic and were only reported to government officials every three or four months (7). Based on the distribution of measurements taken over time, as presented in Muller 1989 (7), the number of measurements tripled in the second period (1968-1977) compared to the earlier period (1958-1967). Thus, the uncertainty caused by variations in radon concentrations in the 1968-1996 period was multiplied by $\sqrt{3}$ to derive an error for the 1958-1967 period.

Estimation of Working Time

From 1967, miners working time was determined using time cards miners filled out daily, which included time spent in each work area underground (1, 7). A similar approach was used in US mines for assigning working time for which an error of 4% was assigned based on an uncertainty of $\pm$ ½ hour in time reporting for an 8-hour shift. Thus, for the period 1967 onward an error of 4% was assigned to the estimation of working time in the Ontario cohort. For the period 1958 to 1967 a general approach for estimating occupancy time was used since miners specific job activities were not recorded. During this period it was assumed that miners spent 80% of their time in work areas (stopes, headings and raises) and 20% in travelways (1, 7, 8). This is often assumed to be a good approximation of the true working time spent by miners underground (Chambers D 2015, personal communication, January 28). Possible changes in working time were then taken into consideration in the calculation of working level months with the introduction of a work history factor that accounted for overtime or work stoppages. Compared to the period from 1968 onward, when personal work times were recorded daily, the period from 1958 to 1967 was assumed to have greater uncertainty since exact times were not recorded and there may be daily fluctuations in the 80/20 ratio. At

minimum, it was assumed that the uncertainty in estimating working time in the period 1954 to 1967 may be double the uncertainty in the latter period to potentially yield an error of 8%.

Precision of the Kusnetz method

The modified Kusnetz method was the most widely used method for measuring radon daughter concentration in Canadian uranium mines (9). This method involves drawing in a known volume of air through a filter for about 5 minutes. The radon daughters on the filter are then left to decay for 40 to 90 minutes and then the alpha activity on the filter is measured using an alpha counter (9, 10). The radon concentration in working levels is then calculated using the equation (10):

$$WL = \frac{C \times (1 + S)}{5F \times t_1 \times K \times E}$$

Where C = total number of counts recorded
S = self-absorption correction for the type of filter used to collect radon progeny
F = flow rate
t_1 = measurement time for alpha activity from the filter
K = the Kusnetz correction/conversion factor
E = counter efficiency

Precision of the Kusnetz method was assessed in Schiager et al. based the ability of the method to accurately detect alpha activity (2). The assessment done by Schiager produced uncertainty estimates of 3-23%, which are dependent on concentration and also the decay time used in the Kusnetz method. However, this precision would have changed over time with improvements made to the modified Kusnetz method, such as modifications to the sampling and counting intervals (10). Another major improvement with the modified Kusnetz method was the use of a scaler instead of a count rate meter used in the basic Kusnetz method, which reduced the limit of detection from 0.3 WL

to 0.03 WL (10, 11). Due to changes in the equipment used with the Kusnetz method, which caused a 10 fold decrease in the limit of detection, as well as modifications made to the Kusnetz method, the uncertainty associated with the Kusnetz method was divided by 10 for the period 1968-1996.

Kusnetz factor

The Kusnetz factor is derived under the assumption that all radon daughters will be in perfect equilibrium, which may not be an adequate reflection of the true ratio at the time of measurement. A Canadian report had estimated inherent method errors, which included both inaccuracies with the Kusnetz factor and data input errors, as having a total error of 5-10% (12). To estimate the error associated solely with the Kusnetz factor, the percentage of error reported by Schiager et al. for data transcription (1.5%) was subtracted from the total inherent errors to derive an estimated error of 3.5-8.5% associated with the use of the Kusnetz factor. This would have been applicable throughout the entire period of uranium mining exposure assessment since there are no documented changes in the Kusnetz factor over time.

Systematic Errors/Human Errors

Systematic errors are those errors typically present in any method including air sample volume errors such as flow rate calibration, filter loading, errors with sample timing, as well as counting errors. A Canadian study comparing the use of personal alpha dosimeters to conventional area monitoring methods, estimated systematic errors to be 5-10% for the Kusnetz method (12). This inherent error source is expected to stay the same across the different periods.

Some systematic errors may occur due to human mistakes in timing or recording values. This was evaluated separately by Schiager et al., as the error associated with the operator in charge of taking

measurements and is presented as a subset of the total systematic errors in Table 1. This can include errors related to timing the sampling interval, timing the decay interval, and reading and recording the number of alpha counts. The total uncertainty assigned to human error for the Kusnetz method would be 2-3% depending on whether the 40 minute decay time or the 90 minute decay time is used. This value was taken from the detailed assessment done by Schiager et al. (2). Since the modified Kusnetz method was used across both periods of sampling, the uncertainty associated with human error is expected to be the same from 1954-1996.

Record Keeping and Data Transcription

Unintentional errors may occur when recording and then further transcribing exposure data from the field and then records. This may include errors in recording or transcribing location code where sample was taken, working level or time spent in each location (2). Schiager et al. (2) estimated that the total amount of error introduced from recording and transcribing discrepancies is 1.5%. A similar number of steps were used in Ontario mines for recording field data and then transcribing them onto IBM cards starting in 1954, which were then transferred to magnetic tape in the 1970s (13) (8). Since a similar number of recording and transcribing steps are involved in the two exposure periods of concern, this error is expected to be the same from 1958-1996.

The total uncertainty from all six sources of exposure was assessed using the root sum square method (2, 3) and was 53.1-67.5% for the earlier period from 1954-1967 and was 31-38% for the period 1968-1996.

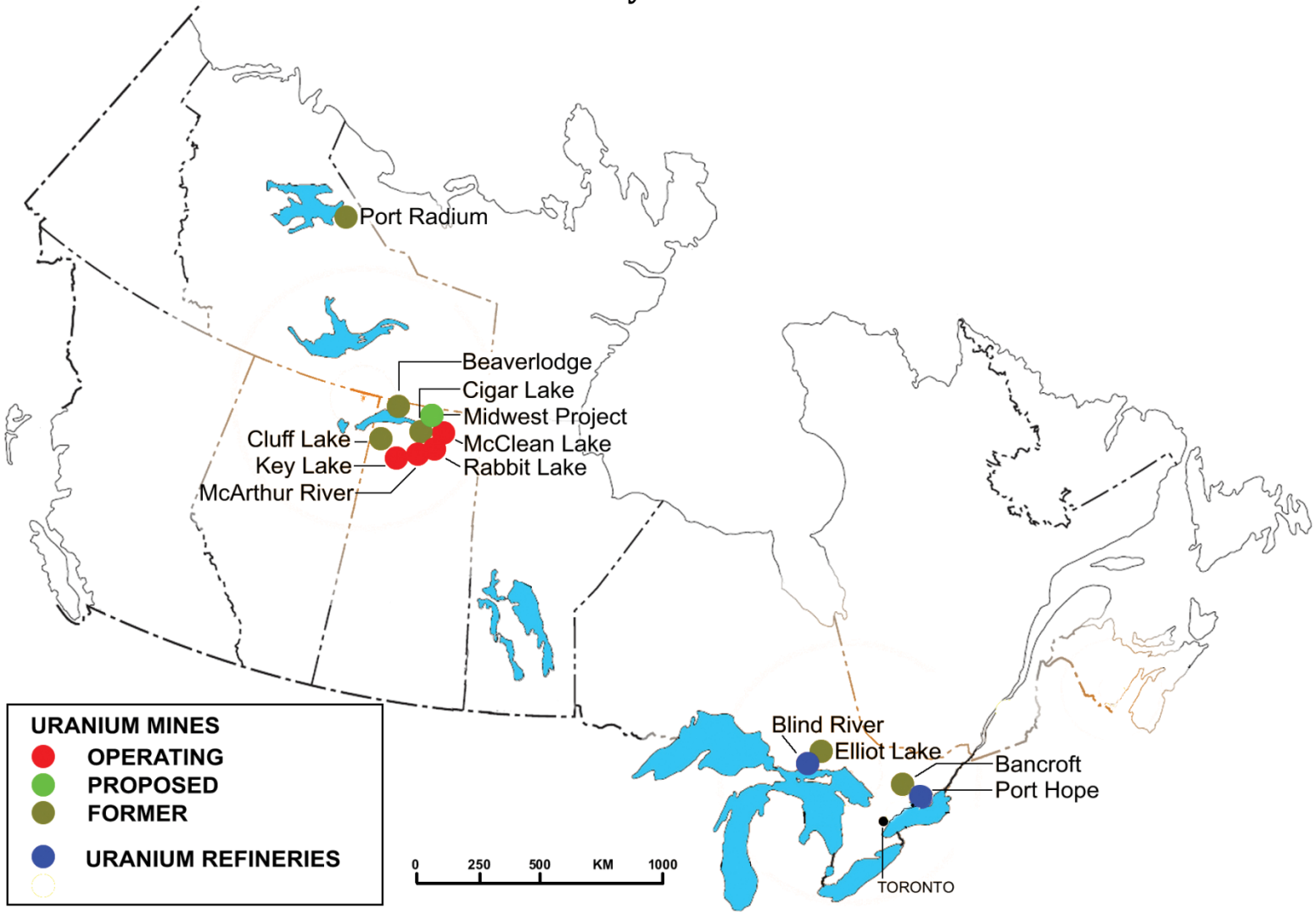
One unique approach used in the Ontario uranium mining industry to assess exposure uncertainty for the earlier period, where doses were thought to be underestimated, was the development of the special and standard working level months to assign exposure by calendar year (1, 7, 8). The standard working level month would be the exposure for a given calendar year derived by taking the average of the three of four month averages reported by companies, whereas the special working level months are the time-weighted averages of the maximum or highest exposures reported by companies to the AECB every few months. However, the effects of these two approaches to assign annual radon doses on the risk estimates was not assessed in this study and could be a future step to assessing exposure uncertainty in a subset of the current cohort.

References

1. United Nations Scientific Committee on the Effects of Atomic Radiation. Effects of Ionizing Radiation: United Nations Scientific Committee on the Effects of Atomic Radiation-UNSCEAR 2006 Report to the General Assembly, with Scientific Annexes C, D, and E. New York, N.Y.: United Nations Publications; 2009. 334 p.
2. Schiager KJ BT, Johnson JA. Radiation monitoring for uranium miners: evaluation and optimization. *ALARA Inc. Final Report on Contract No. J0295026*, 1981.
3. Allodji RS, Leuraud K, Bernhard S, Henry S, Benichou J, Laurier D. Assessment of uncertainty associated with measuring exposure to radon and decay products in the French uranium miners cohort. J Radiol Prot. 2012 Mar;32(1):85-100. PubMed PMID: 22392893. Epub 2012/03/07. eng.
4. Chambers DB, Stager RH, Bernard FD, Lowe LM, editors. Reconstruction of the radon daughter exposure of Beaverlodge uranium workers. Eighth International Congress of the IRPA; 1992; Montreal.
5. Makepeace CE, Stocker H, editors. Statistical interpretation of a frequency of monitoring programme designed for the protection of underground miners from overexposure to radon daughters. International Symposium on Occupational Radiation Exposure in Nuclear Fuel Cycle Facilities; 1979 1979/06/18/. Los Angeles, 18-22 June 1979.
6. Johnson J. Uncertainties in estimating working level months. Atomic Energy of Canada Ltd., Chalk River, Ontario. Chalk River Nuclear Labs, 1978.
7. Muller J, Kusiak RA, Ritchie AC. Factors modifying lung cancer risk in Ontario uranium miners, 1955-1981. Toronto, ON: Ontario Ministry of Labour; Ontario Workers' Compensation Board; Atomic Energy Control Board of Canada, 1989.
8. Muller J, Wheeler WC, Gentleman JF, Suranyi G, Kusiak RA. Study of mortality of Ontario miners 1955-1977, Part I. Toronto and Ottawa: Ontario, Ministry of Labour; Ontario Workers' Compensation Board; Atomic Energy Control Board of Canada, 1983.
9. McPherson MJ. Chapter 13: Radiation and radon gas In Subsurface Ventilation and Environmental Engineering. New Delhi: Springer; 1993. p. 457-88.

10. Atomic Energy Control Board. Guidelines for the Measurement of Airborne Radon Daughters in Mines. Ottawa, ON: Atomic Energy Control Board Canada, 1981 AECB-R 4.
11. International Atomic Energy Agency Safety Series. Manual on Radiological Safety in Uranium and Thorium Mines and Mills. 1976.
12. Balint A, Viljoen J. Comparing personal alpha dosimetry with the conventional area monitoring-time weighting methods of exposure estimation: a Canadian assessment. Atomic Energy Control Board, Ottawa, ON (Canada), 1988.
13. Muller J, Wheeler WC. Causes of death in Ontario uranium miners. Occupational Safety and Health. 1974;32(29):29-42. eng.

Appendix C: Canadian Uranium Mine and Refinery Locations circa 2009



Adapted from Tilman, 2009 (4)