Canadian National Dose Registry of Radiation Workers 1951-2007: Overview of Research

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\textbf{Abstract.} The National Dose Registry (NDR) of Canada is a unique resource for direct estimation of health risks associated with low radiation doses. This is the largest national occupational radiation exposure database, as it includes about 600,000 nuclear, industrial, medical and dental workers exposed to the average cumulative dose of several mSv. Analyses of the NDR data based on a cohort of about 200,000 workers first exposed before 1984 and followed through 1987 and 1988 for mortality and cancer incidence respectively, showed that mortality from most causes of death considered, and cancer incidence were lower than those in the general population, which is typical of occupational cohorts. There was a significant increase over the general population in the incidence of thyroid cancer and melanoma (however, this was not certain to be related to radiation exposure). Significant dose-response was found for mortality from all causes, all cancers, lung cancer, circulatory diseases, accidents, for incidence of all cancers, cancers of the rectum and lung, leukaemia, all cancers except lung and all cancers except leukaemia. In addition, in male workers significant dose-response was found for the incidence of colon, pancreatic and testicular cancers. Estimates of cancer risks based on mortality and incidence were higher than those in most other occupational cohorts and in the Atomic bomb survivors studies. Biologically-based analysis of lung cancer incidence in the NDR showed that for protracted exposure to low radiation doses there was a significant radiation effect on promotion and malignant conversion, but not on the initiation stage of carcinogenesis. This is in contrast to the findings for high-dose acute exposures in Atomic bomb survivors, where initiation and possibly promotion was found to be affected by radiation exposure. An inverse-dose-rate effect, i.e. increase in risk with protraction of a given dose, was found in the NDR cohort.

\textbf{KEYWORDS:} National Dose Registry of Canada, ionizing radiation, low doses, health risks

1. Introduction

Current radiation protection guidelines are largely based on epidemiological studies of the atomic bomb survivors. Extrapolations of health risks from these studies of high dose acute radiation exposures to the much lower doses and dose rates typical of occupational and public exposures are subject to uncertainties. In view of these uncertainties, direct assessment of health risks at low doses and dose rates is of particular importance, and radiation worker studies are the most informative epidemiologic studies of this kind.

The National Dose Registry (NDR) of Canada is a unique resource for direct estimation of health risks associated with low radiation doses. This is the largest national occupational radiation exposure database, which includes radiation exposure information on about 600,000 nuclear, industrial, medical and dental workers exposed to the average cumulative dose of several mSv. Availability of national databases on mortality and cancer incidence in Canada (Canadian Mortality Data Base and Canadian Cancer Incidence Data Base) makes it possible to conduct large-scale epidemiological studies at a relatively low cost by linking the records in the NDR with records in these databases. Since 1983, nearly 30 articles using information from the NDR have been published in scientific journals.

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2. Overview of research in the NDR of Canada

In 1951, the Department of National Health and Welfare established a National Dosimetry Service for monitoring radiation workers in Canada. One of the responsibilities of this new Service was to maintain a system of centralized radiation records, which formed the basis of the National Dose Registry of Canada [1]. At present, the NDR is operated by the Radiation Protection Bureau of Health Canada. In addition to the records of the National Dosimetry Services, it includes records submitted by nuclear power stations, Atomic Energy of Canada Limited, uranium, non-uranium mines, and since the mid-1990s commercial dosimetry companies have contributed data as well.

Thus, the NDR contains records for all monitored radiation workers in Canada (grouped into the following sectors: dental, medical, industrial and nuclear power) on external gamma-, beta-, X-ray and neutron exposures, internal exposures to tritium and radon daughters.

Though the centralized radiation record system was initially intended for regulatory, information and legal purposes, in the following years it became clear that the NDR data could be used for epidemiological analyses of health risks associated with radiation exposure by linking NDR files with mortality and morbidity databases [1-4]. In the 1980’s and early 1990’s, a number of studies were conducted on dosimetry, radiation dose levels, dose distribution and trends in the NDR of Canada [2;5-14]. At the same time, considerable restructures and improvements were made in the NDR database [1-2;15].

The NDR data were first used in an epidemiological case-control study by McLaughlin et al. [16]. This study of paternal radiation exposure and childhood leukemia in the offspring of workers of Ontario nuclear facilities was conducted in response to publications on elevated rates of childhood leukemia in the vicinity of the Sellafield nuclear facility in England and association between the increased risk of childhood leukemia and pre-conception occupational exposure of fathers to ionizing radiation [17]. The study included 112 cases of leukemia diagnosed in the period from 1950 to 1988 in children aged 0-14 born to mothers living in the vicinity of an operating nuclear facility in Ontario, and 890 controls matched by date of birth and residence at birth. Occupational radiation exposure data on fathers of cases and controls were obtained by computerized record linkage with the NDR. No association was found in this study between childhood leukemia and paternal occupational exposure to ionizing radiation before the child’s conception (Odds Ratio 0.87; 95% Confidence Interval (CI): 0.32, 2.34) [16].

The first large-scale epidemiological cohort study was initiated in the early 1990’s. This study involved computerized probabilistic linkage of the radiation dose records of all individuals in the NDR monitored prior to 1984 with records in the Canadian Mortality Database maintained by Statistics Canada [2;15]. The results of this study based on a cohort of nearly 207,000 workers exposed to an average cumulative dose of 6.3 mSv with mortality data through 1987 were published in 1998 [18]. As in many other occupational cohorts, mortality in the NDR was found to be lower than that in the general population, which reflects the healthy worker effect. Standardized Mortality Ratios (SMRs) were significantly less than unity for all causes of death, all cancers combined and a number of individual cancer sites, as well as for most non-cancer causes, including circulatory diseases and accidents. No SMR was significantly increased. At the same time, significant increase in risk with increasing radiation dose was reported in male workers for all causes of deaths (Excess Relative Risk per 1 Sv (ERR/Sv) = 2.5, 90% CI 1.5, 3.5), all cancers (ERR/Sv = 3.0, 90% CI 1.1, 4.9), lung cancer (ERR/Sv = 3.6, 90% CI 0.4, 6.9), cancers in organs other than the lung (ERR/Sv = 2.6, 90% CI 0.3, 5.0), circulatory diseases (ERR/Sv = 2.3, 90% CI 0.9, 3.7) and accidents (ERR/Sv = 8.8, 90% CI 2.7, 15.0). In female workers only ERR for all causes of death was significantly elevated (ERR/Sv = 5.5, 90% CI 0.6, 10.3) [18].

The results of the analysis of cancer incidence in the NDR were published 3 years later [19]. For this analysis, NDR records on about 191,000 workers monitored for radiation exposure between 1969 (the earliest year for which cancer incidence data are available in the Canadian Cancer Data Base) and 1983 were linked with records in the Canadian Cancer Data Base for the period 1969-1988. As in the mortality analysis, cancer incidence in the NDR cohort was found to be lower than that in the general
Canadian population: Standardized Incidence Ratios (SIRs) for all cancers combined and for many specific cancer sites were below unity. However, SIRs for melanoma in males and thyroid cancer in females were significantly elevated. Statistically significant increase with increasing radiation dose was reported in males for all cancers (ERR/Sv = 2.6, 90% CI 1.3, 4.3), lung cancer (ERR/Sv = 3.1, 90% CI 0.6, 7.2), all cancers except lung (ERR/Sv = 2.5, 90% CI 1.0, 4.4), colon cancer (marginally significant ERR/Sv = 2.8, 90% CI 0.0, 8.0), rectal cancer (ERR/Sv = 9.9 90% CI 1.7, 27.4), pancreatic cancer (ERR/Sv = 9.2, 90% CI 0.1, 36.8), testicular cancer (ERR/Sv = 38.3, 90% CI 1.4, 147.9), all cancers except leukemia (ERR/Sv = 2.5, 90% CI 1.1, 4.2) and leukemia (ERR/Sv = 5.9, 90% CI 0.3, 22.7). Associations with radiation exposure for most of these cancers were reported in other occupational cohorts, with the exception of colon cancer and testicular cancer. The ERRs for females could not be estimated with reasonable degree of precision because very few females received higher doses, and there was no clear dose trend.

Trends in occupational radiation doses, cancer and non-cancer mortality (for 1951-1987) and cancer incidence (for 1969-1987) in a cohort of 42,175 Canadian dental workers were studied by Zielinski et al. [20]. Mortality and incidence for most studied health outcomes were lower than in the general Canadian population; the only cancer type with significantly increased incidence was melanoma of the skin (SIR 1.46; 90% CI 1.14, 1.85). The average cumulative dose for dental workers was 0.31 mSv, and there was a marked decrease in occupational radiation doses during the study period in this cohort.

An analysis of mortality for the period 1957-1994 of about 45,500 Canadian nuclear power industry workers from the NDR of Canada monitored for more than 1 year in the period between 1957 and 1994 and exposed to an average cumulative dose of 13.5 mSv was conducted by Zablotska and colleagues [21]. SMRs below unity were reported for all causes of deaths, all cancers, all non-cancer causes and for individual cancers, indicating a substantial healthy worker effect. The estimate of ERR per 1Sv for leukemia excluding chronic lymphocytic leukemia was 52.5 (90% CI, 3.97, 225) and ERR per 1Sv for solid tumours was 2.8 (90% CI, 0.33, 6.32). Of individual cancers, cancer of the oral cavity and pharynx, colon, rectum and lung showed evidence of positive associations with radiation exposure in this analysis. The ERR for rectal cancer, 34.1 per 1 Sv, achieved statistical significance [21]. Canadian nuclear power industry workers were also included in the first international analysis of cancer mortality of 95,000 nuclear workers in Canada, the United States, and the United Kingdom [22] and in the second international analysis of cancer and non-cancer mortality that involved nearly 600,000 nuclear workers from 15 countries [23-27].

There are two classes of statistical models that are employed for analysis of cancer data in radiation epidemiology: empirical and biologically based models [28]. The analyses of mortality and cancer incidence in the NDR of Canada described above, used empirical risk models with the purpose of quantitative estimation of risk from long-term low-level radiation exposures. Recently, biologically-based models (two-stage clonal expansion (TSCE) and extended models) have been applied to lung cancer incidence data in the NDR of Canada in order to get insight into biological processes underlying transformation of somatic cells into malignant cancer cells [29]. This analysis suggests that for protracted exposure to low radiation doses there is a significant radiation effect on promotion and malignant conversion, but not on the initiation stage of carcinogenesis. This is in contrast to the findings for high-dose acute exposures in A-bomb survivors, where initiation [30-31] and possibly promotion [31] were found to be affected by radiation exposure. An inverse-dose-rate effect, i.e. increase in risk with protraction of a given dose was shown for lung cancer in the NDR cohort [29].

Estimates of cancer risks in the NDR of Canada based on both mortality and incidence, though statistically compatible with estimates from some other radiation epidemiology studies, are generally higher than those in most other occupationally exposed cohorts and in the Japanese Atomic bomb survivors. Associations with radiation exposure for non-cancer causes of death, in particular for circulatory diseases and accidents, similar in magnitude to that for cancer, require caution in interpretation of these findings and search for their possible explanations. Of particular concern are possible confounding by non-radiation lifestyle risk factors, potential record linkage errors, and dose uncertainties. To address these concerns, the following studies have been conducted in the NDR cohort.
Linkage errors can arise when some matching records fail to be linked (false negatives), and/or non-matching records are incorrectly linked (false positives). Linkage errors rate in the NDR mortality study [18] was estimated to be 10.9% on the basis of a manual review of 1,756 potential deaths. However, for cohort members classified as being alive, linkage to the summary tax records confirmed the vital status of 99.95%, implying an error rate of only 0.05% for potentially alive individuals. This suggested an overall linkage error rate on the order of 1%. The effect of record linkage errors on risk estimates in cohort mortality studies was investigated by [32]. The theoretical results presented in this paper indicate that false positives not only inflate the observed numbers of deaths, but also tend to deflate the expected numbers of deaths. Conversely, false negatives deflate the observed numbers of deaths and inflate the expected numbers of deaths. Thus, both types of linkage errors introduce bias into estimates of SMRs.

The direction of bias in the relative risk regression coefficients depends on the nature of the regression coefficient. It was also shown that linkage errors introduce additional uncertainty into estimates of both SMRs and regression coefficients [32]. At present, research is underway to develop methods to account for linkage errors in the statistical analyses of actual data.

Dosimetry uncertainties represent an important aspect of epidemiological studies in occupational cohorts. One source of dosimetry uncertainties relevant to the NDR study is the occurrence of large number of dosimeter readings below the detection limit of the radiation dosimeter. Occupational radiation exposures were measured by dosimeters that were read at intervals ranging from 2 weeks to 3 months, and cumulative exposure at a given time was determined by adding all prior exposure measurements. Most radiation dosimeters in Canada have a detection threshold of 0.20 mSv, and all doses below this value are recorded as zero.

The limit of 0.2 mSv was imposed by the National Dosimetry Services (NDS). The dosimeter can read below this value but the dose is likely to be inaccurate after correction for an estimated background. Note that the background can vary from one dosimeter to the next. Today the limit is 0.1 mSv.

This can lead to a significant underestimation of cumulative doses and resulting overestimation of risks associated with occupational radiation exposure [18;33]. In particular, a large proportion (46.7%) of workers included in the mortality study had no recorded exposure, and it was not possible to determine the degree of underestimation of the cumulative dose since the number of doses recorded as zero was not readily available on an individual basis [18].

The effect of this type of dose error (referred to as censoring in recorded exposures) on cancer risk estimates based on the Canadian NDR was studied by Shin et al. [33] who used computer simulation to determine censoring-related bias in excess relative risk estimates. The adverse health outcome considered in this analysis was lung cancer in males. A population was simulated of 96,000 males with known exposure measurements (not subject to censoring) and with lung cancer incidence generated by the ERR model with known ERR. The effect of censoring on estimated ERR was determined by repeatedly simulating data from this population and fitting the ERR model separately to the censored data (obtained by setting any exposure measurements below the detection limit) and the uncensored data. The impact of simulation assumption on the censoring effect was explored by varying three factors in the model and data: the ERR coefficient (0.031%/mSv, 0.31%/mSv and 3.1%/mSv), the lag time between exposure and effect (5, 10 and 15 years) and the frequency of measurements (bimonthly, monthly and quarterly). In order to make the simulation study as realistic as possible, data from the NDR were used to guide the design of the simulation experiments. The study has shown that all the combinations of the three factors resulted in some censoring-induced overestimation of the ERR of lung cancer, and that the most influential factor was measurement frequency. The results of this study suggest that estimates of cancer risk obtained by fitting the ERR model to occupational radiation exposure data are unlikely to be overestimated by more than 15% to 20% [33].

The existing methods for adjustment of recorded doses have been extended by Sont [34] who defined new statistical distributions to improve modelling of low doses of occupational radiation exposure. The maximum likelihood method has been used for parameter estimation and has been adapted so that all
recorded doses can be analyzed as a whole, including doses recorded as zero. This method can be applied to estimate true doses from the complete set of recorded doses.

3. Future plans

We are planning to conduct analyses of mortality and cancer incidence based on an extended cohort that would include more than 550,000 individuals with exposure records in the NDR between 1951 and 2005, and updated mortality and incidence data through 2005. By increasing the follow-up time by up to 18 years, we expect to at least double the number of person-years of observation as well as the number of deaths and incident cancer cases in our extended analysis. These extensions and updates will result in more precise risk estimates of the excess mortality and cancer incidence associated with occupational radiation exposure. We also expect to increase the collective dose for the NDR cohort by about 1,000 Sv with this additional follow-up. Our future analyses will account for dosimetry uncertainties, in particular random measurement error and error introduced by dosimetry detection limit. These analyses together with updates and improvements made to personal identifiers in the NDR cohort file and improvements to the estimates of recorded doses made after the initial analyses, will contribute to better estimates of risk.

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REFERENCES:


