CANADIAN NATIONAL DOSE REGISTRY OF RADIATION WORKERS: OVERVIEW OF RESEARCH FROM 1951 THROUGH 2007

JAN M. ZIELINSKI1,2, NATALIA S. SHILNIKOVA3, and DANIEL KREWSKI2,3

1 Health Canada, Ottawa, Canada
Healthy Environments and Consumer Safety Branch
2 University of Ottawa, Ottawa, Canada
Department of Epidemiology and Community Medicine, Faculty of Medicine
3 University of Ottawa, Ottawa, Canada
McLaughlin Centre for Population Health Risk Assessment
Institute of Population Health

Abstract
The National Dose Registry (NDR) of Canada is a unique resource for a direct estimation of the potential health risks associated with low doses of ionizing radiation. This is the largest national occupational radiation exposure database, comprising records for about 600,000 nuclear, industrial, medical and dental workers. An analysis 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, revealed that the mortality from most causes of death considered was lower than that in the general population, which is typical of occupational cohorts. Although the same was also observed for cancer incidence, there was a significant increase in the incidence of thyroid cancer and melanoma which, however, was not clearly related to radiation exposure. A significant dose-response was found for mortality from all causes, all cancers, lung cancer, cardiovascular 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, a significant dose-response was found for the incidence of colon, pancreatic, and testicular cancers. The estimates of cancer risks (mortality and incidence) were higher than those in most other occupational cohorts and in the studies on atomic bomb survivors. The biologically based dose-response models used to describe lung cancer incidence in the NDR showed that for a protracted exposure to low radiation doses there was a significant radiation effect on the promotion and malignant conversion, but not on the initiation stage of carcinogenesis. This stands in contrast to the findings for high-dose acute exposures in A-bomb survivors, where the initiation and possibly promotion were found to be affected by radiation exposure. Evidence of an inverse dose-rate effect (i.e. an increase in the risk with a protraction of a given cumulative dose) was found in the NDR cohort.

Key words:
National Dose Registry of Canada, Ionizing radiation, Low doses, Health risks

INTRODUCTION
Current radiation protection guidelines are based largely on epidemiological studies of the atomic bomb survivors. The 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 a number of uncertainties. Therefore, direct assessments of health risks at low doses and dose rates are needed; the studies on radiation workers provide an opportunity to address this need. The National Dose Registry (NDR) of Canada is a unique resource for a direct estimation of potential health risks associated with low doses of ionizing radiation. This is the largest national database on occupational radiation exposure.
exposure, which includes information on about 600 000 nuclear, industrial, medical and dental workers exposed to the average cumulative dose of several mSv. The availability of the national databases on mortality and cancer incidence in Canada makes it possible to conduct large-scale epidemiological studies, at a relatively low cost, by linking the records in the NDR with the records in these databases. Since 1983, nearly 30 articles using information from the NDR have been published in scientific journals.

OVERVIEW OF NDR RESEARCH

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 the new Service was to maintain a system of centralized radiation dose 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 Ltd., uranium and non-uranium mines, and, since the mid-1990s, commercial dosimetry companies. The NDR contains records for virtually all radiation workers in Canada monitored for external gamma, beta, X-ray and neutron exposures, as well as internal exposures to tritium and radon daughters.

Though the centralized radiation dose record system was initially intended for informational, regulatory, and legal purposes, it soon became clear that the NDR data could be used for epidemiological analyses of the potential health risks associated with radiation exposure, by linking the NDR files with the mortality and morbidity databases [1–4]. In the 1980’s and early 1990’s, a number of reports on dosimetry, radiation dose levels, and dose distribution and trends in the NDR of Canada were published [2,5–14]. At the same time, the NDR database was subject to restructuring and improvement [1–2,15].

The NDR data were first used in an epidemiological case-control study by McLaughlin et al. [16]. The authors studied the paternal radiation exposure and childhood leukemia in the offspring of workers of the Ontario nuclear facilities. The project was conducted in response to the publications on elevated rates of childhood leukemia in the vicinity of the Sellafield nuclear facility in England, and a possible association between the increased risk of childhood leukemia and pre-conception occupational exposure of fathers to ionizing radiation [17]. The study [16] comprised 112 cases of leukemia diagnosed between 1950 and 1988 in children aged 0–14 years born to mothers living in the vicinity of an operating nuclear facility in Ontario, and 890 controls matched by the date of birth and residence at birth. Data on occupational radiation exposure of the fathers of cases and controls were obtained by a 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 (OR = 0.87, 95% CI: 0.32, 2.34) [16].

The first large-scale epidemiological cohort study was initiated in early 1990’s. This study involved a computerized probabilistic linkage of the radiation dose records of all individuals in the NDR monitored prior to 1984 with the records in the Canadian Mortality Database maintained by the Statistics Canada [2,15]. The results of this study, which was based on a cohort of nearly 207 000 workers exposed to an average cumulative dose of 6.3 mSv with a mortality follow-up through 1987, were published in 1998 [18]. As in many other occupational cohorts, mortality in the NDR study group was found to be lower than that in the general population, which reflects the healthy worker effect. The standardized mortality ratios (SMRs) were significantly lower than unity for all causes of death, all cancers combined, and a number of individual cancer sites. The mortality from non-cancer causes, including cardiovascular diseases and accidents, was also lower than that in the general population. No SMR was significantly increased. At the same time, a significant increase in the risk with an 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), cardiovascular 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 exposure, which includes information on about 600 000 nuclear, industrial, medical and dental workers exposed to the average cumulative dose of several mSv. The availability of the national databases on mortality and cancer incidence in Canada makes it possible to conduct large-scale epidemiological studies, at a relatively low cost, by linking the records in the NDR with the records in these databases. Since 1983, nearly 30 articles using information from the NDR have been published in scientific journals.
National Dose Registry of Canada: An Overview

Zablotska and colleagues conducted an analysis of mortality for the period of 1957–1994 for about 45,500 Canadian nuclear power industry workers registered in the NDR who were exposed to an average cumulative dose of 13.5 mSv and monitored for more than 1 year within the study period [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/Sv for leukemia, excluding chronic lymphocytic leukemia, was 52.5 (90% CI: 3.97, 225) and ERR/Sv for solid tumours was 2.8 (90% CI: 0.33, 6.32). Among individual cancers, the 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 Sv, reached statistical significance [21]. The 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 the analysis of cancer data in radiation epidemiology: the empirical and biologically based models [28]. The analyses of mortality and cancer incidence in the NDR cohort described above were based on the empirical risk models used for a quantitative estimation of risk from long-term low-level radiation exposures. Recently, the biologically based models (including the two-stage clonal expansion (TSCE) model of carcinogenesis and the extended versions of this model) have been applied at the NDR to analyze lung cancer incidence data in order to gain insight into the biological processes underlying the transformation of somatic cells into malignant cancer cells [29]. The results of this analysis suggest that for a protracted exposure to low radiation doses, there is a significant radiation effect on the promotion and malignant conversion, but not on the initiation stage of carcinogenesis. This stands in contrast to the findings for high-dose acute exposures in A-bomb survivors, where the initiation [30–31] and possibly promotion [31] were found to be affected by radiation.

The results of the analysis of cancer incidence in the NDR cohort were published three 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 the 1969–1988 data in the Canadian Cancer Data Base. As in the mortality analysis, the cancer incidence in the NDR cohort was found to be lower than that in the general Canadian population: the standardized incidence ratios (SIRs) for all cancers combined and for many specific cancer sites were below unity. However, the SIRs for melanoma in males and for thyroid cancer in females were significantly elevated. A statistically significant increase in cancer risk with an 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 a reasonable degree of precision because very few females received higher doses, and there was no clear dose trend.

The trends in occupational radiation exposures, and the associated mortality (for 1951–1987) and cancer incidence (for 1969–1987) in a cohort of 42,175 Canadian dental workers were examined by Zielinski et al. [20]. The mortality and incidence for most of the studied health outcomes were lower than in the general Canadian population; the only cancer type with a significantly increased incidence was skin melanoma (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.
exposure. An inverse dose-rate effect, i.e. an increase in the risk with a protraction of a given cumulative dose, was found for lung cancer in the NDR cohort [29].

In the NDR of Canada, the estimates of cancer risks based both on mortality and incidence, though statistically compatible with the 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. The associations with radiation exposure for the non-cancer causes of death, in particular for cardiovascular diseases and accidents, are similar in magnitude to those for cancer in the NDR cohort, while in the atomic bomb survivors, the estimates of the ERR/Sv are considerably lower for the non-cancer causes as compared to cancer mortality [32]. For these reasons, a caution in interpreting the NDR risk estimates is advised. A particular concern in this respect is the possibility of confounding by non-radiation lifestyle risk factors, as well as the possible record linkage errors, and uncertainties in radiation dose measurements. To address these concerns, a number of studies have been conducted in the NDR. The results of these studies are described in the sections below.

The linkage errors can arise when some matching records fail to be linked (false negatives), and/or non-matching records are incorrectly linked (false positives). In the NDR mortality study [18], the linkage error rate, estimated based on a manual review of 1756 potential deaths, was found to be 10.9% (false positives and false negatives combined). However, for the cohort members classified as being alive, the linkage to the summary tax records confirmed the vital status of 99.95%, implying an error rate of only 0.05% for the potentially alive individuals. This suggested an overall linkage error rate of the order of 1%. The effect of the record linkage errors on the risk estimates in the cohort mortality studies was investigated by Krewski and co-workers [33]. The theoretical results presented in this paper indicate that the false positives not only inflate the observed numbers of deaths, but also tend to deflate the expected numbers of deaths. Conversely, the false negatives deflate the observed numbers of deaths and inflate the expected numbers of deaths. Thus, both the types of linkage error introduce bias into SMR estimates. The direction of bias in the regression coefficients of relative risk depends on the nature of the regression coefficient. It was also shown that the linkage errors introduce additional uncertainty into the estimates of both SMRs and regression coefficients [33]. At present, research is underway to develop methods to account for the linkage errors in the statistical analyses of actual data.

Uncertainties in radiation dosimetry represent an important aspect of epidemiological studies in occupational cohorts. One source of a dosimetric uncertainty relevant to the NDR study is the occurrence of a large number of dosimeter readings below the detection limit of the radiation dosimeter. The occupational radiation exposures were measured by dosimeters that were read at intervals ranging from two weeks to three months, and the cumulative exposure at a given time was determined by adding all prior exposure measurements. Most radiation dosimeters in Canada had a detection threshold of 0.20 mSv, and all doses below this value were recorded as zero. The limit of 0.2 mSv was imposed by the National Dosimetry Services (NDS). The dosimeter could read below this value but the dose was likely to be inaccurate after correction for an estimated background. Note that the background can vary from one dosimeter to the next. Today, the detection threshold is 0.1 mSv.

The circumstances described above could lead to a significant underestimation of the cumulative doses and the resulting overestimation of risks associated with occupational radiation exposure [18,34]. 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 of recorded exposures) on cancer risk estimates based on the Canadian NDR was studied by Shin et al. [34] who used computer simulation to determine the censoring-related biases in excess relative risk estimates. The adverse health outcome considered in this analysis was lung cancer in males. A population of 96,000 males was simulated with known exposure measurements (not subject to censoring)
and with lung cancer incidence generated by the ERR model with a known ERR. The effect of censoring on the estimated ERR was determined by repeatedly simulating the 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 the simulation assumptions on the censoring effect was explored by varying three factors in the model and data: the ERR coefficient (0.031%/mSv, 0.31%/mSv, or 3.1%/mSv), the time lag between exposure and effect (5, 10 or 15 years), and the frequency of measurements (bimonthly, monthly, or quarterly). In order to make the simulation study as realistic as possible, the data from the NDR were used to guide the design of the simulation experiments. The study demonstrated 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 the frequency of measurements. The results of this study suggest that the 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% [34].

The existing methods for the adjustment of the recorded doses have been extended by Sont [35] who defined the new statistical distributions to improve the modelling of low doses of occupational radiation exposure. The maximum likelihood method was used for parameter estimation, and has been adapted so that all the recorded doses can be analyzed as a whole, including the doses recorded as zero. This method can be applied to estimate the true doses from the complete set of the recorded doses.

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 the 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 1000 Sv with this additional follow-up. Our future analyses will take account of the dosimetry uncertainties, in particular the random measurement error and the error introduced by the dosimetry detection limit. These analyses, together with the updates and improvements made to personal identifiers in the NDR cohort file and the improvements to the estimates of recorded doses made after the initial analyses, will contribute to better estimates of the risks associated with occupational exposure to ionizing radiation based on NDR records.

CONCLUSION

The National Dose Registry of Canada is the largest national registry of occupational radiation exposures in the world, and represents a valuable resource for investigating the potential adverse health effects of long-term low-level exposure to ionizing radiation. Although data from the Japanese cohort of atomic bomb survivors currently serve as the primary basis for the radiation protection standards developed by the International Commission on Radiological Protection (ICRP) [36], the occupational radiation exposure data, such as that provided by the NDR, should also be considered in setting these standards. However, the differences between the risk estimates based on the NDR cohort and the A-bomb survivors (with the NDR providing notably higher risk estimates) need to be addressed. At the same time, the epidemiological follow-up in the NDR of Canada should be continued, and the results of such studies taken into account when developing future radiation protection standards.

ACKNOWLEDGEMENTS

Daniel Krewski is the NSERC/SSHRC/McLaughlin Chair in Population Health Risk Assessment at the University of Ottawa. This work was supported in part by a grant from the Canadian Institutes of Health Research.
REFERENCES


